American Heart Journal

VOL. 38 DECEMBER, 1949 No. 6

Original Communications

ATRIAL SEPTAL DEFECT. A STUDY OF INTRACARDIAC SHUNTS, VENTRICULAR OUTPUTS, AND PULMONARY PRESSURE GRADIENT

JOHN B. HICKAM, M.D.
DURHAM, N. C.

PATIENTS with atrial septal defect provide an unusual opportunity for the study of certain problems connected with the regulation of cardiac output and the hemodynamics of the pulmonary circulation. It is frequently possible to pass a catheter through the septal defect into the venous side of the pulmonary circulation. Blood samples and pressure determinations from this site extend the significance of the usual observations which can be made in the course of an intracardiac catheterization. It is possible to determine the pressure gradient through the pulmonary vascular tree, to estimate the right and left ventricular outputs, to estimate the magnitude and direction of intracardiac shunts, and to observe changes in some of these quantities as a result of exercise or other stimuli. This paper reports observations on four patients with atrial septal defect in whom it was possible to catheterize pulmonary veins.

METHODS

Intracardiac catheterization was performed by a method previously described.[1] Oxygen consumption was measured by timed collection of expired air in Douglas bags, volume measurements in a Tissot spirometer, and analysis in the Haldane apparatus. Blood samples for oxygen analysis were collected under oil with oxalate as an anticoagulant or were drawn into oiled, heparinized syringes and stored in ice. Oxygen analyses were carried out by the method of Van Slyke. Duplicate analyses were required to check within 0.1 volume per cent. In Case 2, blood oxygen contents were determined by a spectrophotometric method.[2] Pressure measurements in the heart were made through the catheter by Hamilton manometer, the point of zero reference being taken as 5.0 cm.

From the Department of Medicine, Duke University School of Medicine, Durham, N. C.
This work was supported by grants from the Life Insurance Medical Research Fund and the Anna H. Hanes Fund of Duke University.

below the fourth costochondral junction. Mean pressures were determined by planimetry. Arterial blood was obtained from the brachial artery through an inlying needle. All determinations were made while the patient was in a supine position. Exercise was carried out by alternately flexing and extending both legs together at a constant rate. No determinations were made until exercise had been continued for at least three minutes. Exercise studies were preceded by observations made at rest during the same catheterization. In the case of J. C. (Case 3) the pulmonary venous pressure and oxygen content of pulmonary venous blood reported during exercise were determined at the same study in a separate exercise period, which resembled as closely as possible the exercise period during which the remaining determinations were made.

CASE HISTORIES

CASE 1.—A. L., a white man, 37 years old, had noticed as a child that he was unusually short of breath on exertion. In the last ten years exertional dyspnea had gradually become worse and for two years there had been frequent episodes of lower respiratory tract infection and a chronic cough. He had not had ankle edema. Examination showed moderate cyanosis. The fingers were clubbed. The heart was moderately enlarged. The rhythm was regular. Along the left sternal border in the third to fifth intercostal spaces there was a low-pitched, long diastolic murmur of moderate intensity. Roentgenograms showed an enlargement of the pulmonary conus and a dilatation of the pulmonary arteries, that on the left being of aneurysmal proportions. The diagnosis of atrial septal defect was made by intracardiac catheterization (see Table 1).* Two months later the left pulmonary aneurysm was wrapped with Cellophane. At the time of the second catheterization, one year later, the patient's symptoms and physical findings were substantially unchanged, except that there had been a decrease in the frequency and severity of respiratory infections.

CASE 2.—N. Q., a white girl, 12 years of age, had been entirely asymptomatic. She was referred for study after discovery of a heart murmur in a routine examination. There was a precordial systolic murmur maximal in the second and third intercostal spaces at the left sternal border. The pulmonary conus was enlarged, and the vascular markings at the lung roots were accentuated. There was right axis deviation. The figures were not clubbed.

CASE 3.—J. C., a white diabetic man, 31 years old, had had moderate nonprogressive exertional dyspnea for many years. Seven years before the present study, examination disclosed a harsh systolic murmur maximal in the pulmonic area and transmitted down the left sternal border. The pulmonic second sound was louder than the aortic. Roentgenograms showed prominence of the pulmonary conus and the pulmonary vascular markings. There was right axis deviation. The fingers were not clubbed, and there was no cyanosis. At the time of the present study there had been no significant change in these findings. The diagnosis of atrial septal defect was made by intracardiac catheterization.

CASE 4.—C. D., a Negro man, 24 years old, had been well until three years before the present study. At that time he developed pain in both knees, lasting two to three weeks. Shortly thereafter he began to have brief spells of unconsciousness, unrelated to posture. For a time these were frequent, but there had been none for six months before study. For six to eight months there had been slowly progressive exertional dyspnea. There was a transient episode of ankle edema. Examination showed moderate clubbing of the fingers. There was a prominent pulsation of the neck veins with cardiac systole. Fluoroscopy showed generalized cardiac enlargement, including both atria, and increased pulmonary vascular markings. There was complete heart block with a ventricular rate of 32 to 36 per minute and right axis deviation. The pulmonary

*The first study was conducted by Dr. James V. Warren of Emory University, who has kindly made the data available.

second sound was accentuated. Over the precordium there was a harsh, blowing systolic murmur. At the apex a low-pitched diastolic murmur was inconstantly heard. On the basis of these findings and observations made during intracardiac catheterization, the diagnoses of atrial septal defect and possible mitral disease were made.

OBSERVATIONS

The data obtained by intracardiac catheterization of these patients are presented in Table I. Calculations made from the data appear in Table II.

Calculations.—In determining percentage saturation no correction is made for dissolved oxygen. The accuracy of the measurement in this study is not sufficient to warrant such a correction. For reasons of economy, blood for oxygen capacity was not drawn with each appropriate sample. The values for percentage saturation are therefore to be regarded as approximate. For example, the figure of 100 per cent for percentage saturation of pulmonary venous blood in A. L. (Case 1) is clearly incorrect. Here, the result has been taken to indicate normal oxygenation of the blood, and a pulmonary venous saturation of 97 per cent[3] has accordingly been used for calculating results in the preceding study on this patient. This approximation involves little error in subjects with a large arteriovenous difference across the lungs, but would not be admissible in the ordinary case, where the A-V difference is quite small (see the following).

The right ventricular output in cases of atrial septal defect is obtained by dividing the oxygen consumption by the arteriovenous difference across the lungs:

$$RVO\ (Liters\ per\ minute) = \frac{O_2\ consumed\ (cubic\ centimeters\ per\ minute)}{Pulmonary\ venous\ oxygen\ content - pulmonary\ arterial\ oxygen\ content\ (cubic\ centimeters\ per\ liter)}$$

This calculation assumes that pulmonary collateral circulation is insignificant.

The left ventricular output can be approximated by dividing the oxygen consumption by the arteriovenous difference across the heart:

$$LVO\ (Liters\ per\ minute) = \frac{O_2\ consumed\ (cubic\ centimeters\ per\ minute)}{Arterial\ oxygen\ content - mixed\ caval\ oxygen\ content\ (cubic\ centimeters\ per\ liter)}$$

This equation neglects the contribution from the coronary sinus. The exact mixed caval content is, of course, not available. However, data of Brannon and co-workers[4] indicate that the oxygen contents of superior and inferior caval blood in cases of atrial septal defect at rest do not usually vary by more than 1.0 vol. per cent. Accordingly, the superior caval oxygen content was used in estimating the resting left ventricular output, except in Case 2, in which values for superior and inferior caval blood are averaged. Such an approximation would not be valid for subjects carrying out leg exercise. No estimate of left ventricular output during exercise is possible from the data presented in Table I.

Because of the probability of a small right-to-left shunt and the possibility of coexistent pulmonary vascular disease, calculation of the right ventricular

TABLE I

CASE	STATE	SURFACE AREA (SQ. M.)	O_2 CONSUMPTION (C.C. PER MIN.)	PRESSURE (MM. HG)									BLOOD OXYGEN CONTENT (VOL. PER CENT)								
				RIGHT ATRIUM	LEFT ATRIUM	PULMONARY VEIN	PULMONARY ARTERY			SYSTEMIC ARTERY			SUPERIOR VENA CAVA	RIGHT ATRIUM	LEFT ATRIUM	PULMONARY VEIN	PULMONARY ARTERY	SYSTEMIC ARTERY	SATURATION	SATURATION ARTERIAL BLOOD	PER CENT SATURATION PULMONARY VENOUS BLOOD
							SYSTOLIC	DIASTOLIC	MEAN	SYSTOLIC	DIASTOLIC	MEAN									
A. L.	Rest	1.59	215	0.5*	1.0*		113†			116	68	79	14.3	14.4	21.9		17.5†	22.0	25.4	87	
	Rest[1]	1.60	183	4	6	6	93	50	65	96	63	78	14.2	14.2	20.3	22.8	15.8	18.2	22.8	80	"100"
N. Q.	Rest	1.16	188	3		4	22	9	16				11.5[2]	15.0		15.8	14.9	15.6	16.2	96	98
J. C.	Rest	1.60	269	6		7	30	9	20	132	81	101	11.4	13.0		16.7	14.9	15.7	18.0	87	93
	Exercise		457	2		5	36	12	23	151	84	113	14.5			16.9	14.2	16.6		92	94
C. D.	Rest[3]		306	18			52	14	25	145	95	115	12.5	17.0			18.2	19.8	21.8	91	
	Rest	1.73	239	16		19	58	8	23	158	93	120	11.1	16.7		20.1	18.5	19.6	22.6	87	89
	Exercise		536	30			95	23	45	184	92	125					15.2	19.3		85	

*Saline manometer.
†Right ventricle.

[1]One year after first study.
[2]Inferior vena caval blood: 11.8 vol. per cent.
[3]Separate study.

TABLE II

CASE	STATE	LEFT VENTRICULAR OUTPUT (L. PER MIN.)	RIGHT VENTRICULAR OUTPUT (L. PER MIN.)	PULMONARY PRESSURE GRADIENT (MM. HG)	PULMONARY RESISTANCE (PULMONARY GRADIENT PER RIGHT VENTRICULAR OUTPUT) (MM. HG PER L. PER MIN.)	RIGHT-TO-LEFT SHUNT (L. PER MIN.)	LEFT-TO-RIGHT SHUNT (L. PER MIN.)	$\frac{1\text{-}X^*}{Y\dagger}$	EFFECTIVE PULMONARY FLOW (L. PER MIN.)
A. L.	Rest	2.8	3.2[1]			0.7	1.0	.34	2.2
	Rest[2]	4.6	2.6	59	22.7	2.4	0.5	.65	2.1
N. Q.	Rest	4.7	19.8	12	0.61	0.2	15.3	.23	4.5
J. C.	Rest	6.3	14.9	13	0.87	1.2	9.8	.56	5.1
	Exercise		16.9	18	1.06			.11	
C. D.	Rest[3]	4.2							
	Rest	2.8	14.9	4	0.27	0.2	12.2	.33	2.7
	Exercise[4]		10.9	12	1.10			.16	

*1-X = Fraction of aortic blood which is caval in origin.
†Y = Fraction of pulmonary arterial blood which is caval in origin.
[1]Assuming pulmonary venous blood to be 97% saturated (see text).
[2]One year later.
[3]Separate study.
[4]Calculations utilize resting pulmonary venous oxygen.

output should employ data from pulmonary venous blood rather than arterial blood or an assumed value for normal saturation. With a large right ventricular output the arteriovenous difference across the lungs may be quite small, and an error in its determination will produce a relatively large error in the output estimation. Since the left ventricular output is usually much smaller than the right, a similar error in estimating oxygen content of mixed caval blood will produce a much smaller absolute error in estimation of the left ventricular output. For example, C. D. (Case 4) at rest had a right ventricular output of 14.9 liters per minute and a left ventricular output of 2.8 liters per minute. An error of 1.0 vol. per cent in estimation of pulmonary venous oxygen content would yield a right ventricular output of 9.2 or 39.8 liters per minute, while a similar error in estimating mixed caval oxygen content would yield a left ventricular output of 2.5 or 3.2 liters per minute, depending upon the direction of error.

Calculation of the shunts may be made from the general formulas presented by Dexter and associates.[5] For the present specific problem a simpler treatment appears adequate. Each side of the heart may be considered separately. The aortic blood is a mixture of pulmonary venous blood and of caval blood, from the right-to-left shunt. If the oxygen content of blood from these two regions be known, as well as the oxygen content of the mixture in the aorta, one can determine what fraction of the aortic mixture is caval in origin. Let $1-X$ be the caval fraction; the remainder, X, will then be the pulmonary fraction. Let the oxygen content of aortic blood be A, caval blood VC, and pulmonary venous blood PV. The composition of A as a mixture can then be described as

$$A = (1-X)VC + X\,PV.$$

Solving for X,

$$X = \frac{A-VC}{PV-VC},$$

and for $1-X$,

$$1-X = \frac{PV-A}{PV-VC}.$$

The minute volume of the right-to-left shunt is the product of the caval fraction and the left ventricular output, $(1-X)\,(LVO)$.

In a similar way, the oxygen content of pulmonary arterial blood, PA, results from a mixture of pulmonary venous blood and caval blood. If $(1-Y)$ be the fraction of the pulmonary arterial blood contributed by the pulmonary veins, then the remainder, Y, will be the fraction which is caval in origin. Again,

$$PA = (1-Y)PV + YVC.$$

Solving for Y,

$$Y = \frac{PV-PA}{PV-VC},$$

and for $1-Y$,

$$1-Y = \frac{PA-VC}{PV-VC}.$$

The minute volume of the left-to-right shunt is the product of the pulmonary fraction and the right ventricular output, $(1-Y)\,(RVO)$.

The effective pulmonary flow, as defined by Bing,[6] is estimated from the expression $\frac{O_2\ consumption}{PV-VC}$. This represents the flow rate of caval blood which passes through the pulmonary bed, and is therefore equal to $Y(RVO)$. It is also that portion of the left ventricular output which is contributed from the pulmonary veins and is therefore equal to $X(LVO)$.

The data are inadequate for calculation of shunts during exercise because there is no information as to the oxygen content of the mixed caval blood. However, an index of change in the proportional values of the shunts is provided by the expression $\frac{1-X}{Y} = \frac{PV-A}{PV-PA}$, that is, the ratio of the caval fraction of the aortic blood to the caval fraction of the pulmonary arterial blood. A decrease in this ratio indicates a decrease in the proportional size of the shunts, that is, a decrease in right-to-left shunt, a left-to-right shunt, both shunts together, or a proportional fall in one shunt large enough to mask a rise in the other. The interpretive value of this ratio is quite limited, but a change in the ratio does indicate a change in the proportional value of the shunts.

Interatrial Shunts and Ventricular Outputs.—The existence of a large left-to-right shunt in patients with atrial septal defect has long been regarded as reasonably certain,[7,8] but direct evidence for the shunt was first provided by Brannon and associates,[4] who found large quantities of oxygenated blood entering the right atrium. This observation has been amply confirmed. The existence of a small right-to-left shunt is indicated by the present data. This has been suspected clinically and was anticipated by Cournand from an analysis of pressure curves in the two atria during the cardiac cycle.[9]

There is almost no information on changes in ventricular outputs and shunts in response to various stimuli. The occurrence of cyanosis in congestive failure and on exercise in some patients has been taken to indicate an increased right-to-left shunt.[8] However, Burchell and Wood[10] suggest that this may result, in cyanotic forms of congenital heart disease, from a fall in oxygen content of the shunted venous blood rather than an increase in the shunt itself. They have found that venous shunts in a variety of anatomic conditions have remained remarkably constant for each patient under varying environmental conditions of stress and over a period of time. This is apparently not always the case in atrial septal defect. The shunts of A. L. (Case 1) changed significantly between the two studies. The data on J. C. (Case 3) and C. D. (Case 4) indicate a change in absolute as well as proportional values of the shunts from rest to exercise. Proportional change in shunts is indicated by the changes in the ratio $\frac{1-X}{Y}$, which fell during exercise in each case. Other considerations indicate that the absolute values must have changed, as well. In J. C. (Case 3) exercise produced no significant change in pulmonary venous oxygen or right ventricular output, but a rise in systemic arterial oxygen almost to the pulmonary venous level.

This combination of events can result only from a change in the absolute quantity of shunted blood. In the case of C. D. (Case 4) the total right ventricular output during exercise falls below the resting left-to-right shunt, clearly indicating a considerable decrease in the latter during exercise.

The right ventricular outputs of J. C. and C. D. are quite large at rest. During exercise there is little change in the right ventricular output of J. C., while there is a definite fall in that of C. D. In J. C. there was a definite fall in right atrial pressure during exercise, and in C. D. a very large rise, indicating that changes in right ventricular output were not primarily dependent on changes in atrial pressure. Atrial pressures could not be controlled by determination of the intrathoracic pressure, but it seems doubtful that atrial pressure changes of these magnitudes could result from intrathoracic pressure changes alone, with only a moderate increase in pulmonary ventilation. In normal man, exercise and pulmonary ventilation of this extent produce no significant change in atrial pressure.[11] The left ventricular outputs during exercise are not yielded by the data. Clinical evidence would suggest that they increased. In general, patients who have not been in frank failure and are able to walk at a moderate rate without discomfort will show an increase in cardiac output on mild exercise.[11] In the case of C. D. a separate study indicated that the left ventricular output could be increased, at least moderately (Table II).

In summary, there is evidence that proportional and absolute values of the shunts can change spontaneously and in response to exercise; that the change during exercise in two cases was in the direction of an over-all decrease in the proportional magnitude of the shunts; that the right ventricular output may fall or remain substantially unchanged during exercise in the face of a probable rise in the left ventricular output; and that changes in right ventricular output can be independent of changes in right atrial pressure. These findings suggest that the dynamics of atrial septal defect are not determined simply by atrial pressure levels.

Dexter[12] and Cournand[9] have found that left atrial and pulmonary venous pressures in hearts with atrial septal defect are slightly higher than right atrial pressures, and this is confirmed by the present results. It has been suggested that this pressure differential is the cause of the shunt.[7,8] It would appear, however, that if the shunt exists, the pressure differential must exist and that more information is needed before positions of cause and effect are assigned. It is possible (1) that the normal filling pressures of the two ventricles are different; (2) that atrial pressure is an important factor in setting the level of the cardiac output; (3) that other factors affect output of the two ventricles to a roughly comparable degree, and, therefore; (4) when the two atria communicate, that ventricle which normally operates under the lower pressure more readily accepts the available blood and has the larger output. Information is still inadequate on the first and third of these propositions. On the other side, there is adequate evidence that the cardiac output in man may vary widely without apparent relation to the atrial pressure, and that, in fact, the atrial pressure level in many situations is not the dominant factor in determining the cardiac output.[13] The unequal ventricular outputs in atrial septal defect could well depend upon some factor other than atrial pressure. In this case the predominant shunt and the atrial pressure gradient would be secondary to the difference in ventricular outputs. No conclusive evidence supports either view. The present study of

changes in ventricular outputs and shunts indicates that the dynamics of hearts with atrial septal defects are not determined simply by atrial pressure levels.

The Pulmonary Pressure Gradient.—Although the pulmonary arterial pressure can be determined easily in man by intracardiac catheterization, direct determinations of pulmonary venous pressure are ordinarily not possible. For this reason, interpretation of pulmonary vascular changes by means of changes in pulmonary arterial pressure is uncertain. In congestive heart failure the problem arises as to whether high pulmonary arterial pressures, increasing on exercise, are to be ascribed to a rise in pulmonary vascular resistance, to elevation of left atrial pressure, or to both. The same problem exists with the slight changes in pulmonary pressure sometimes seen in normal individuals during exercise. In the more marked changes described by Motley and co-workers[14] for normal subjects during anoxia, the magnitude of the pressure rise and parallel studies in animals[15] suggest that an increase in pulmonary vascular resistance does occur.

In the present study the opportunity arose to make observations on the pulmonary pressure gradient (that is, the difference in pressure between pulmonary artery and vein) in four subjects, with a comparison of the gradient at rest and exercise in two subjects. The determination of the gradient should be unaffected by the intrapleural pressure, since this presumably has an equal influence on the measurement of atrial and pulmonary arterial pressures. The data obtained are presented in Table I, and the pressure gradient and "pulmonary resistance," in Table II. The calculation of pulmonary resistance is made, according to Aperia,[16] in terms of the ratio of mean pressure to flow, but the resistance is expressed in millimeters of mercury per liter per minute, rather than in absolute units. Pulmonary resistance is used in an attempt to compensate for pressure changes which result from changes in volume flow. A rise in this figure is taken to indicte pulmonary vascular constriction, while a fall indicates dilatation or opening of new channels. The ability of normal man to increase greatly the pulmonary blood flow during exercise with minimal increase in pulmonary arterial pressure[13] suggests that pulmonary resistance normally falls during exercise.

Three of the subjects show some degree of pulmonary hypertension at rest, while one (N. Q.) does not. N. Q. was able to pass approximately 20 liters per minute through the pulmonary bed under a pressure gradient of 12 mm. of mercury.

In J. C. one-third of the pulmonary arterial pressure (7.0 mm.) and in C. D. 5.6 of the pressure (19 mm.) was contributed by the pulmonary venous pressure. In both cases the pulmonary blood flow was large. The resistance of J. C. (0.87 mm. Hg per liter per minute) is probably near normal; that of C. D. (0.27 mm. Hg per liter per minute) is extremely low. This patient, with an atrial septal defect and possible mitral disease, was able to pass 15 liters of blood per minute through the pulmonary circulation under a pressure gradient of only 4.0 mm. of mercury. Pressure tracings from C. D. are shown in Fig. 1. In A. L., by contrast, there is considerable pulmonary hypertension (mean pressure 65 mm. Hg), to which the pulmonary venous pressure makes a relatively insignificant contribution. The pulmonary flow is quite low with a resultant high resistance (22.7 mm. Hg per liter per minute), about eighty times that of C. D. Pressure tracings from this patient appear in Fig. 2. Obliterative pulmonary arterial disease has been described in patients with atrial septal defect.[7,8,17]

Pulmonary hypertension in A. L. appears to be on the basis of arterial disease; in C. D. it results entirely from transmitted left atrial pressure. In the three patients without evident pulmonary vascular disease very large flow rates can be maintained through the pulmonary bed under an extremely low pressure gradient. This great distensibility emphasizes the degree to which pulmonary vascular disease must progress before pulmonary hypertension appears at rest in subjects with a normal pulmonary flow.

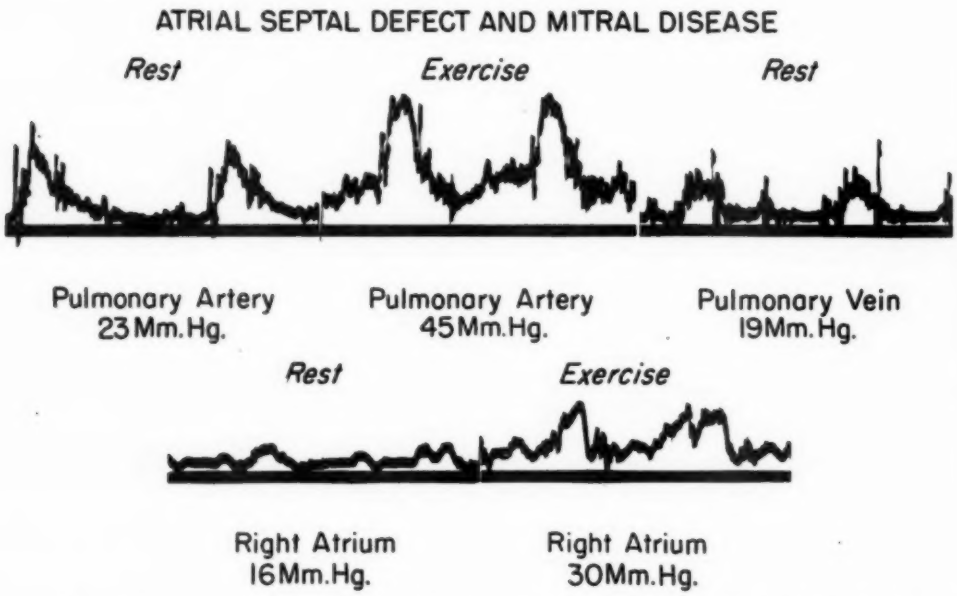


Fig. 1.—Intracardiac pressure tracings from C. D., with atrial septal defect and possible mitral disease. Indicated pressures are mean values. Tracings illustrate the large contribution to pulmonary arterial pressure made by the atrial pressure at rest and during exercise in a subject with pulmonary vascular engorgement.

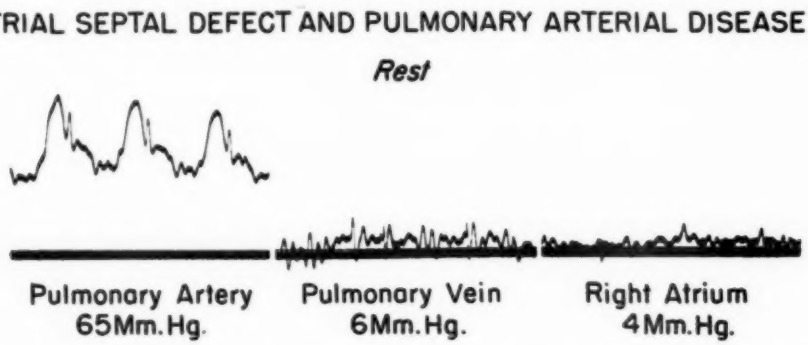


Fig. 2.—Intracardiac pressure tracings from A. L., with atrial septal defect and pulmonary vascular disease. Indicated pressures are mean values. Tracings illustrate pulmonary hypertension based on a high pulmonary vascular resistance.

During exercise, the resistance rose in both J. C. and C. D. In the former, the rise was only 20 per cent; in the latter, 300 per cent. In C. D. the pulmonary venous pressure was not measured during exercise but was estimated to be 3.0 mm. Hg higher than the right atrial pressure, as at rest. It was probably no higher because the left-to-right shunt decreased during exercise. A lower figure would give even a greater increase in gradient and a greater resistance during exercise.

The effect of exercise on the pulmonary circulation of C. D. is of particular interest. In certain respects the findings are similar to those of a subject with left ventricular failure; the pulmonary arterial pressure is elevated at rest and becomes still more elevated during exercise in spite of a decreased pulmonary blood flow.[13] In this case the abnormal elevation of pulmonary arterial pressure at rest proves to be based on a high pulmonary venous pressure. The small pressure difference between artery and vein suggests a widely dilated pulmonary vascular tree. On exercise, the pulmonary arterial pressure is doubled. The major part of the rise in arterial pressure results from a rise in pulmonary venous pressure. However, the gradient is tripled, and there is a fourfold increase in pulmonary resistance. An opposite result might have been expected from passive dilatation of the vascular tree by increased pressure through its whole course. It is not clear whether the increase in pulmonary vascular resistance results from arteriolar constriction, narrowing of the capillary lumen by edema of the vessel wall, or some other mechanism. The result does suggest that the pulmonary hypertension of exercise in subjects with pulmonary vascular engorgement may result largely from an increased pulmonary venous pressure, but also may be caused in some part by an increased pulmonary vascular resistance.

SUMMARY AND CONCLUSIONS

1. Data are presented on four patients with atrial septal defect in whom it was possible to extend the usual intracardiac catheterization studies by entering the pulmonary veins and, as a result, to estimate the separate ventricular outputs and intracardiac shunts and to determine the pulmonary pressure gradient and pulmonary vascular resistance.

2. The proportional and absolute values of the intracardiac shunts can change spontaneously and in response to exercise. During exercise, changes in right and left ventricular outputs may not parallel each other and may even be opposite in direction. Changes in right ventricular output may be opposite in direction to changes in right atrial pressure.

3. The pulmonary pressure gradient and right ventricular output were measured in four subjects at rest, and in two during exercise. In two subjects with apparently normal pulmonary vessels the pulmonary vascular resistance was extremely low (0.6 to 0.9 mm. Hg per liter per minute). These subjects maintained pulmonary blood flows of 15 to 20 liters per minute under pressure gradients of 12 to 13 mm. of mercury. One subject with pulmonary vascular engorgement had a pulmonary flow of 15 liters per minute with a pressure gradient of only 4.0 mm. of mercury.

4. During exercise the subject with pulmonary vascular engorgement developed pulmonary hypertension. This was primarily due to an increase in left atrial pressure, but there was also a significant rise in the pressure gradient and in the pulmonary vascular resistance.

REFERENCES

1. Stead, E. A., Jr., Warren, J. V., Merrill, A. J., and Brannon, E. S.: The Cardiac Output in Male Subjects as Measured by the Technique of Right Atrial Catheterization. Normal Values With Observations on the Effect of Anxiety and Tilting, J. Clin. Investigation **24**:326, 1945.
2. Hickam, J. B., and Frayser, R.: Spectrophotometric Determination of Blood Oxygen Content, J. Biol. Chem. **180**:457, 1949.
3. Roughton, F. J. W., Darling, R. C., and Root, W. S.: Factors Affecting the Determination of Oxygen Capacity, Content and Pressure in Human Arterial Blood, Am. J. Physiol. **142**:708, 1944.
4. Brannon, E. S., Weens, H. S., and Warren, J. V.: Atrial Septal Defect. Study of Hemodynamics by the Technique of Right Heart Catheterization, Am. J. M. Sc. **210**:480, 1945.
5. Dexter, L. D., Haynes, F. W., Burwell, C. S., Eppinger, E. C., Seibel, R. E., and Evans, J. M.: Studies of Congenital Heart Disease. I. Technique of Venous Catheterization as a Diagnostic Procedure, J. Clin. Investigation **26**:547, 1947.
6. Bing, R. J., Vandam, L. D., and Gray, F. D.: Physiological Studies in Congenital Heart Disease. I. Procedures, Bull. Johns Hopkins Hosp. **80**:107, 1947.
7. Roesler, H.: Interatrial Septal Defect, Arch. Int. Med. **54**:339, 1934.
8. Bedford, D. E., Papp, C., and Parkinson, J.: Atrial Septal Defect, Brit. Heart J. **3**:37, 1941.
9. Cournand, A., Motley, H. L., Himmelstein, A., Dresdale, D., and Baldwin, J.: Recording of Blood Pressure From the Left Auricle and the Pulmonary Veins in Human Subjects With Interauricular Septal Defect, Am. J. Physiol. **150**:267, 1947.
10. Burchell, H. B., and Wood, E. H.: Physiologic Measurements in Cardiac Malformations, Mod. Concepts Cardiovasc. Dis. **17**:25, 1948.
11. Hickam, J. B., and Cargill, W. H.: Effect of Exercise on Cardiac Output and Pulmonary Arterial Pressure in Normal Persons and in Patients With Cardiovascular Disease and Pulmonary Emphysema, J. Clin. Investigation **27**:10, 1948.
12. Dexter, L., Haynes, F. W., Burwell, C. S., Eppinger, E. C., Sosman, M. C., and Evans, J. M.: Studies of Congenital Heart Disease. III. Venous Catheterization as a Diagnostic Aid in Patent Ductus Arteriosus, Tetralogy of Fallot, Ventricular Septal Defect, and Auricular Septal Defect, J. Clin. Investigation **26**:561, 1947.
13. Stead, E. A., Jr., Hickam, J. B., and Warren, J. V.: Mechanism for Changing the Cardiac Output in Man, Tr. A. Am. Physicians **60**:74, 1947.
14. Motley, H. L., Cournand, A., Werkö, L., Himmelstein, A., and Dresdale, D.: The Influence of Short Periods of Induced Acute Anoxia Upon Pulmonary Artery Pressures in Man, Am. J. Physiol. **150**:315, 1947.
15. Liljestrand, G.: Regulation of Pulmonary Arterial Blood Pressure, Arch. Int. Med. **81**:162, 1948.
16. Aperia, A.: Hemodynamical Studies, Skandinav. Arch. f. Physiol. Suppl. 16 to vol. **83**:35, 1940.
17. Massee, J. C.: Atrial Septal Defect, Correlation of Autopsy Findings With Data Obtained by Right Heart Catheterization, Am. J. M. Sc. **214**:248, 1947.

CARDIAC DYSFUNCTION IN HYPERTHYROIDISM

A Study of 810 Cases

Dwight Griswold, M.D., and John H. Keating, Jr., M.D.

New York, N. Y.

CARDIAC insufficiency and arrythmias are common in hyperthyroidism. When associated with this condition, they lend themselves to permanently successful therapy more often than when found in conjunction with organic heart disease. Because cardiac insufficiency and arrythmia can be terminated in such a high proportion of cases, further study of cardiac dysfunction in hyperthyroidism seems warranted.

The cardiovascular complications of the hypermetabolic state were first noted by Caleb Parry in 1786, as described in his unpublished writings.[1,2] Then in the latter half of the 1830's Graves and Basedow[1] both described the association of cardiovascular symptoms and exopthalmic goiter. Similar notes are known to have been made by Stokes[1] in 1854 and Potain[1] in 1863.

In retrospect, the true cause and effect relationship of hyperthroidism on cardiac function was made clearer by Trousseau's error[1] in 1863 when he gave tincture of iodine in place of tincture of digitalis to a patient suffering from cardiac failure. On discovering his error he stopped the iodine, whereupon the cardiac symptoms of his patient worsened. (The clinical significance of iodine was not realized until sixty years later.) In 1879 Lockridge[3] proposed the term "cardiac exophthalmic goiter."

In 1896 Moebius[1] accented the importance of the involvement of the circulatory system in thyroid disease, and three years later Kraus[1] presented the toxic theory of exophthalmic goiter. Various abnormalities in the myocardial conduction system in thyrotoxicosis were shown visually by electrocardiographic tracings in 1918.[4]

The first extensive series of cases studied was in 1922,[5] when it was observed that a large number of patients past middle life exhibited various conduction defects. In 1923 a review was published[6] showing that partial or complete relief of cardiac failure could be achieved in a plurality of patients by thyroidectomy. In that same year the concept was propounded[7] that the development of auricular fibrillation was dependent more on the duration than on the severity of the increased metabolic state. Other observers[8] agreed with this concept.

Periodically since these original papers, there have been more extensive clinical studies evaluating the cardiovascular state in patients with hyperthyroidism. At times there has been controversy over the interpretation of the results, but certain basic clinical facts are agreed upon. These will be incorporated in the discussion that follows.

From the Department of Medicine, St. Luke's Hospital, New York, N. Y.

From the pathologic standpoint early observers disputed the occurrence of specific myocardial lesions in those cases of hyperthyroidism with cardiovascular involvement. In 1921 Goodpasture[9] reported two cases showing myocardial necrosis, and these clinical findings were reproduced in animal experiments.[10] Other authors[11,12] also found focal myocardial degeneration. However, the present-day concept, expressed by Hellwig,[13] Rake,[14] and Kepler and Barnes,[15] is that there are no primary histologic myocardial changes resulting from hyperthyroidism.

From the physiologic standpoint, there is a common belief[16,17,18] that the circulation of the blood is accelerated and that the cardiac output is increased to enable the transport of larger quantities of oxygen to the overactive tissues of the thyrotoxic patient. This additional burden, if untreated, will lead to cardiac insufficiency, especially in the presence of associated organic heart disease. In 1941, after careful animal experimentation, Rasmussen[19] expressed a conflicting opinion: that the principal deleterious effect of the thyroid hormone on the heart and circulation is not the creation of extra work owing to the increased oxygen transport, but is its influence on cardiac rhythm. Thyroid hormone in excess, he believes, causes functional heart disease, of which the essential feature is paroxysms of tachycardia, leading to failure. From this he argues that tachycardia is not a mechanism of circulatory adjustment but is a condition in itself detrimental to the heart and circulatory system.

The roentgenographic appearance of the heart has likewise been the subject of controversy. The minority[20] believe that the cardiac silhouette is characteristically that of a "ham heart," due to a high aortic arch and an increased prominence of the superior vena cava and pulmonary conus. The majority[21,22] hold that there is no physiognomic silhouette and that cardiac enlargement shows a direct relationship to age and coincident cardiovascular disease. Yet it is conceded that there may be the picture of the so-called "ham heart" in some cases uncomplicated by organic heart disease and of sufficient duration of the toxic state. Gotta[21] expresses still another viewpoint, that the prominence of the pulmonary conus is purely of constitutional origin and not the result of hyperthyroidism.

The consensus is that there are no consistent electrocardiographic patterns peculiar to thyrotoxicosis. A variety of changes in T waves and RS-T segments, as well as the presence of auricular fibrillation, auricular flutter, and both A-V and bundle branch block, have been reported.[24-27] Detailed discussion is outside the province of this paper.

With this historical review in mind, a series of 810 patients with hyperthyroidism admitted to the ward and private services of St. Luke's Hospital between 1927 and 1947 were reviewed. Those with borderline signs and symptoms were excluded.

In this report patients with either persistent auricular fibrillation or signs of cardiac insufficiency on admission were classified as thyrocardiacs, whether or not there was associated organic cardiovascular disease. Those with hyperthyroidism who did not meet these standards were classified as nonthyrocardiacs and were used as controls.

Admittedly, paroxysmal tachycardia, paroxysmal fibrillation, and extrasystoles are the most common cardiac manifestations of hyperthyroidism, but the accurate evaluation of these arrythmias in such a survey is not feasible. Moreover, they do not enter into the arbitrary criteria of the thyrocardiac.[18,28]

ANALYSIS OF THE MATERIAL

General.—Of the 810 cases, 103 (12.5 per cent) were thyrocardiacs. Table I outlines the method of their treatment. Those cases listed in the operative column as being treated with either x-ray therapy or thiouracil received them as a definitive measure. Because symptoms were not relieved, operation followed.

TABLE I. METHOD OF TREATMENT OF 103 THYROCARDIACS

Total operative cases	72	Total nonoperative cases	31
Operation alone	62	X-ray therapy	10
X-Ray therapy followed by operation	9	Radium	1
Thiouracil followed by operation	1	Thiouracil	4
		No treatment*	16

*Includes those who died before treatment was instituted and those who refused treatment.

The seventy-two thyrocardiacs surgically treated had an operative mortality of 6.9 per cent. Six thyrocardiacs died as a result of cardiovascular complications before definitive treatment could be instituted, either operative or conservative. There were 623 nonthyrocardiacs operated upon, with a mortality of 2.2 per cent, which for the past ten years alone has been 1.4 per cent. Any death within ten days of surgery was considered an operative mortality. The greater operative risk to thyrocardiacs was also found at the Lahey Clinic,[29] where the figure 6.6 per cent was reported when comparable standards were used. The reason for the greater operative hazard among thyrocardiacs will become evident as the discussion develops. The incidence of carcinoma of the thyroid among the surgically treated individuals with hyperthyroidism was 0.3 per cent.

Sex Distribution.—Table II presents the data on sex distribution.

TABLE II. SEX DISTRIBUTION

	THYROCARDIAC	NONTHYROCARDIAC	TOTAL
Men	26	106	132
Women	77	601	678
Total	103	707	810

Of the 103 thyrocardiacs, 25 per cent were men, and 75 per cent women. On the other hand, among the nonthyrocardiacs there were 15 per cent men and 85 per cent women. From these figures it is seen that whereas fewer men are afflicted with hyperthyroidism, they are more likely to have cardiovascular complications.

Average Age.—The age of thyrocardiacs on admission averaged 51 years, whereas that of the nonthyrocardiacs averaged 41 years. In order to account

for the age difference between the two groups, it may be postulated that the cardiovascular system of thyrocardiacs, already impaired by the expected degenerative process of an additional ten years, is more susceptible to the toxic influence of the thyroid hormone. The age of male thyrocardiacs averaged 47 years, and of female, 54. The average age among the nonthyrocardiacs in each sex was ten years less. There is no satisfactory explanation for the fact that men in both groups are consistently younger than women.

An analysis was made which compared the age of the patients to the type of gland. It was found, both in thyrocardiac patients and nonthyrocardiac control patients, that patients of both sexes with toxic nodular glands were, on the average, approximately ten years older than those with toxic diffuse glands. An explanation of this difference may rest on a previous observation[30] that many of the patients with toxic adenomata have a prolonged or intermittent subclinical course. This in turn would delay diagnosis, in contradistinction to the early diagnosis of those with diffuse goiters who have a more explosive course.

Symptom Duration.—A difference was found in the median duration of toxic symptoms between thyrocardiacs (13.1 months) and controls (10.8 months). Among the thyrocardiacs there was no significant difference in symptom duration either between men and women or between types of gland, although men and patients with diffusely enlarged glands experienced slightly shorter duration of symptoms before treatment. The control group did exhibit significant difference in that men had a shorter duration of symptoms than women. Moreover, those individuals with diffusely enlarged glands were ill for a shorter period before treatment than patients with adenomatous glands.* Three thyrocardiacs did not exhibit outward evidence of thyrotoxicosis, and to them the term "masked hyperthyroidism," as used by Likoff and Levine,[28] is applied. In these instances the cardiac signs and symptoms overshadowed those of hyperthyroidism.

Symptoms of cardiac dysfunction in thyrocardiacs were evident for a median duration of eight months. In this group, however, individuals with toxic adenomata had noticed symptoms for twice as long as those with toxic diffuse glands. Again there was no difference in symptom duration between the sexes in relation to the type of gland. That the duration of thyrotoxicosis may play a part in the development of cardiac dysfunction is reflected by the fact that the duration of symptoms in the thyrocardiacs was significantly longer than in the controls. These findings are in agreement with other reports.[30-32]

Thyrocardiac Classification.—Among the 103 thyrocardiacs there were 44 per cent with toxic nodular glands (six men and thirty-nine women), and 56 per cent with hyperplastic glands (twenty men and thirty-eight women). In comparison, among the controls there were 34 per cent with toxic nodular glands and 66 per cent with hyperplastic glands. Although in our group of thyrocardiacs there was about equal dispersion between toxic nodular and hyperplastic glands, there has been dispute on this point in the literature,[33,34] to the effect that the incidence of toxic nodular glands among thyrocardiacs is higher.

*In every case the frequency was broken at 11.8 months, the median of the over-all distribution.

Coexisting Cardiovascular Disease.—On the basis of clinical and laboratory investigation, 755 cases could be classified as to the presence or absence of coexisting cardiovascular disease. Of ninety-eight thyrocardiacs, 52 per cent had associated cardiovascular disease, compared with 13 per cent in the 657 controls. Clearly seen is the influence of organic disease on the production of cardiac manifestations in thyrotoxicosis. Despite the fact that the thyrocardiacs were ten years older, on an average, than the controls, the incidence of organic heart disease among them is higher than would be expected in their age group. However, attention should be called to the fact that as many as 48 per cent of thyrocardiacs had no demonstrable organic heart disease.

Types of Coexisting Cardiovascular Disease.—Table III presents the analysis of patients with coexisting cardiovascular disease. With the exception of the higher incidence of arteriosclerotic heart disease in this series, the results closely approximate the study of Likoff and Levine.[28]

TABLE III. COEXISTING CARDIOVASCULAR DISEASE IN HYPERTHYROID PATIENTS

TYPE OF DISEASE	THYROCARDIAC		NONTHYROCARDIAC	
	CASES	PER CENT	CASES	PER CENT
Arteriosclerotic heart disease	21	42	15	18
Hypertensive cardiovascular disease	20	40	54	64
Combined arteriosclerotic and hypertensive cardiovascular disease	3	6	2	2
Rheumatic heart disease	6	12	14	16
Totals	50	100	85	100

Influence of Coexisting Cardiovascular Disease on Cardiac Insufficiency in Thyrocardiacs.—From Table IV the influence of associated cardiovascular disease on cardiac insufficiency is evident. Of those patients in failure, thirty-six had coexisting cardiovascular disease and eighteen had none demonstrable.

TABLE IV. COEXISTING CARDIOVASCULAR DISEASE AND CARDIAC INSUFFICIENCY

	PATIENTS WITH CARDIOVASCULAR DISEASE	PATIENTS WITHOUT CARDIOVASCULAR DISEASE
No failure	14	30
Failure	36	18
Minimal*	20	10
Moderate†	12	5
Severe‡	4	3
Totals	50	48

**Minimal*: One or more of the following: Basal râles, ankle edema, or pulmonary congestion indicated by x-ray study.

†*Moderate*: The status between the two extremes.

‡*Severe*: Orthopnea, hydrothorax, hepatomegaly, massive edema, and so forth.

When cardiac failure was considered, there were fifty-four cases of cardiac insufficiency. The distribution between sexes is interesting, because only 32 per cent of the male thyrocardiacs, compared to 60 per cent of the female thyrocardiacs, had signs of cardiac insufficiency. A greater percentage of male thyrocardiacs in failure would be expected, since in the past the greater intensity of hyperthyroidism among men in comparison to women has been generally noted.[35-37] It has also been emphasized[31,32] that the development of cardiac complications may depend on the intensity of the disease. However, in this series, the percentage of men in failure was small. Furthermore, there was no apparent difference in the severity of thyrotoxicosis, as measured by signs, symptoms, and elevated basal metabolic rate, between thyrocardiacs and non-thyrocardiacs.

Cardiac Rhythm and Failure.—Persistent auricular fibrillation on hospital admission was present in the majority of thyrocardiacs, as is shown in Table V. No significant difference between the two types of glands was found in women. In men, the small number of cases obviates comparison. Among the fifty-four patients with congestive failure, thirty-five (65 per cent) had accompanying auricular fibrillation. This figure is appreciably lower than the more than 90 per cent previously reported.[38] In agreement with Slesinger,[39] no relationship appeared between the severity of the thyrotoxicosis and development of the auricular fibrillation. Of the thirty-five patients with both congestive failure and auricular fibrillation, twenty-three had associated cardiovascular disease and twelve had none demonstrable. The greater frequency of cardiac failure in the presence of organic heart disease is consistent. In comparison, thirty-seven patients had auricular fibrillation without failure.

TABLE V. THE INCIDENCE OF AURICULAR FIBRILLATION IN THYROCARDIACS

	MEN	MEN WITH AURICULAR FIBRILLATION	WOMEN	WOMEN WITH AURICULAR FIBRILLATION	TOTAL WITH AURICULAR FIBRILLATION	PER CENT OF TOTAL WITH AURICULAR FIBRILLATION
Nodular	6	4	39	27	31	69
Diffuse	20	16	38	25	41	71
Totals	26	20	77	52	72	70

Although cardiac decompensation in the presence of normal sinus rhythm and in the absence of demonstrable independent cardiac disease is said to be a rarity,[40] ten such examples were found in this series.

Adequate postoperative data were available for thirty-six individuals who had persistent auricular fibrillation. Of these, twenty reverted to sinus rhythm—twelve within one month, six within six months, and two within eighteen months. The remaining sixteen did not revert while under observation. Twelve were observed for more than six months. Since quinidine was used in only one case, the rate of spontaneous reversion to sinus rhythm (53 per cent) was in accord with the findings of Anderson.[41] However, he found that with the use of quinidine in the immediate postoperative period, reversion to normal rhythm occurred in more than 90 per cent of the patients. That reliance on spontaneous reversion should not be depended upon is also stressed by others.[38,42]

The incidence of transitory postoperative auricular fibrillation among nonthyrocardiacs was 4.2 per cent. This figure is slightly higher than that quoted by Means.[43] A theory[44] to explain the cause of postoperative auricular fibrillation is that, following thyroidectomy, there is a rise in the basal metabolic rate for the first twenty-four hours, mainly as the result of fever and anxiety. One would suppose that auricular fibrillation would be a more frequent complication among nonthyrocardiac patients who had coexisting cardiovascular disease than among those without it. But in this series only 23 per cent of those with postoperative auricular fibrillation had associated cardiovascular abnormalities.

Precordial Pain.—Among thyrocardiacs there were 11 per cent who complained of angina, whereas in the controls there were only 3.5 per cent. The ratio of men to women was 3 to 1 in the former and 4 to 1 in the latter.

Electrocardiographic Study.—A total of 556 patients had electrocardiographic studies. No consistent patterns were established in either group. Compatible with their being in a higher age group and having a greater incidence of associated cardiovascular disease, thyrocardiacs appeared to have more frequent abnormalities than did the controls.

Follow-up.—Fifty-six thyrocardiacs were followed for an average of four and one-half years. Table VI shows the distribution of the follow-up.

TABLE VI. LENGTH OF THYROCARDIAC FOLLOW-UP

YEARS	NUMBER OF CASES
0-1	10
1-2	7
2-5	19
5-10	11
10-13	9
Total	56

The follow-up in Table VII shows the high proportion of excellent results in this type of heart disease. A probable explanation for the unfavorable results in the patients treated by x-ray is that their poor operative risk warranted only conservative therapy. For the same reason those patients treated with thiouracil, not shown in the table, made little improvement. Of the five so treated, four were followed, one of whom later came to operation and obtained complete relief of symptoms.

TABLE VII. RESULTS OF FOLLOW-UP OF THYROCRADIACS IN FAILURE ON ADMISSION

	OPERATIVELY TREATED	X-RAY TREATED
Patients regaining and maintaining compensation	24	1
Patients regaining and not maintaining compensation	1	0
Patients not regaining compensation	7	4
Total patients followed	32	5

Of the thirty-seven individuals with persistent auricular fibrillation and without cardiac decompensation, sixteen were followed postoperatively and showed no cardiac insufficiency during the average follow-up period of four and one-half years. In the control group, 184 patients were followed a minimum of five years. Five of these became decompensated on an average of ten years postoperatively, and one suffered a myocardial infarct after five years.

It is of some consequence that once a thyrocardiac has regained compensation following treatment, he is no more likely to suffer similar subsequent episodes than is a patient in the control group.

SUMMARY AND CONCLUSIONS

Certain important points should be reviewed to summarize the foregoing analysis and discussion. Despite the greater operative hazard among thyrocardiacs in failure, there are few other diseases leading to cardiac insufficiency that can be treated with so high an expectation of a return to normal.

In this study a group of patients with hyperthyroidism who did not exhibit either persistent auricular fibrillation or cardiac insufficiency were used as controls. Whenever possible, comparisons were drawn between them and the thyrocardiacs.

That the severity of hyperthyroidism does not play an etiological role in the production of a thyrocardiac has been illustrated. Indeed, three patients in failure in this series showed no outward evidence of hypermetabolism. The postoperative alleviation of their apparent myocardial disease is proof of the validity of this concept.

In the presence of hyperthyroidism in this series, the pathologic state of the gland, adenomatous or diffuse, could not be correlated with the development of cardiac manifestations.

The one phenomenon that may not revert to normal (with operative interference alone), in the majority of cases, is persistent auricular fibrillation. In these patients the use of quinidine postoperatively is a necessity for insuring a successful outcome.

The factors of age, sex, duration of the thyrotoxic state, and coexisting cardiovascular disease all appear to play a part in the production of an abnormal cardiac status: age, inasmuch as thyrocardiacs are, on the average, ten years older than their counterparts; sex, as men are more likely to become thyrocardiacs but less prone to develop failure; duration of symptoms, since it would seem that the longer the hyperthyroid state is allowed to proceed unchecked, the more probable becomes the development of cardiac signs and symptoms; and coexisting cardiovascular disease, which in this series is present in 52 per cent of thyrocardiacs as compared to 13 per cent of the controls. Its role as an agent in the etiology of cardiac insufficiency becomes apparent when one realizes that this condition was present in twice as many of the patients in failure as in those not in failure.

In spite of all these apparently definite causative factors, it must be stressed that in any one case, no prerequisites need be fulfilled for the development of the thyrocardiac state.

We are indebted to Dr. J. W. Fertig and Miss L. R. Elveback of the School of Public Health, Columbia University, for reviewing the statistical material in this paper.

REFERENCES

1. Ginsburg, A. M.: The Historical Development of the Present Conception of Cardiac Conditions in Exophthalmic Goiter, Ann. Int. Med. **5**:505, 1931.
2. Phillips, J., and Anderson, J. P.: Cardiac Disturbances in Goiter, J. A. M. A. **89**:1380, 1927.
3. Lockridge, J. E.: Graves' Disease, or Cardiac Exophthalmic Goiter, Am. Practitioner **9**:287, 1879.
4. Krumbhaar, E. B.: Electrocardiographic Observations in Toxic Goiter, Am. J. M. Sc. **155**:175, 1918.
5. Hamilton, B. E.: Clinical Notes on Hearts in Hyperthyroidism, Boston M. & S. J. **86**:216, 1922.
6. Hamilton, B. E.: Thyroidism Complicated by Heart Failure, J. A. M. A. **80**:1771, 1923.
7. Williams, F. A., Boothby, W. M., and Wilson, L. B.: The Heart in Exophthalmic Goiter and Adenoma With Hyperthyroidism, M. Clin. North America **7**:189, 1923.
8. Lahey, F. H., and Hamilton, B. E.: Thyrocardiacs: Their Diagnostic Difficulties: Their Surgical Treatment, Surg., Gynec. & Obst. **39**:10, 1924.
9. Goodpasture, E. W.: Myocardial Necrosis in Hyperthyroidism, J. A. M. A. **76**:1545, 1921.
10. Goodpasture, E. W.: The Influence of Thyroid Products on the Production of Myocardial Necrosis, J. Exper. Med. **34**:407, 1921.
11. Lewis, W.: The Question of a Specific Myocardial Lesion in Hyperthyroidism (Basedow's Disease), Am. J. Path. **8**:255, 1932.
12. Goodall, J. S., and Rogers, L.: The Nature of Thyrotoxic Myocarditis, Lancet **1**:486, 1927.
13. Hellwig, C. A.: The Goiter Heart, Arch. Surg. **48**:27, 1944.
14. Rake, G., and McEachern, D.: A Study of the Heart in Hyperthyroidism, Am. Heart J. **8**:19, 1932.
15. Kepler, E. J., and Barnes, A. R.: Congestive Heart Failure and Hypertrophy in Hyperthyroidism: A Clinical and Pathological Study of 178 Fatal Cases, Am. Heart J. **8**:102, 1932.
16. Blumgart, H., and Gargle, S.: The Adaptation of the Circulation to Hyperthyroidism and to Hypothyroidism, J. Clin. Investigation **6**:18, 1928.
17. Burwell, C. S., Smith, W. C., and Neighbors, DeW.: The Output of the Heart in Thyrotoxicosis With a Report of a Case of Thyrotoxicosis, Am. J. M. Sc. **178**:157, 1929.
18. Hurxthal, L. M.: The Thyrocardiac, Frank Howard Lahey Birthday Volume, Springfield, Ill., 1940, Charles C Thomas, Publisher, p. 245.
19. Rasmussen, H.: Influence of the Thyroid Hormone on Heart and Circulation, Acta med. Scandinav. (Suppl.) **115**:1, 1941.
20. Cookson, H.: The Size and Shape of the Heart in Goitre, Proc. Roy. Soc. Med. **25**:1517, 1932.
21. Hurxthal, L. M., Menard, O. J., and Bogan, M. E.: The Size of the Heart in Goiter, Am. J. M. Sc. **180**:772, 1930.
22. Hawley, S. J.: A Roentgen Study of the Chest in 200 Patients With Goiter, Am. J. Roentgenol. **32**:326, 1934.
23. Gotta, H.: Size and Shape of the Heart in Hyperthyroidism, Arch. Int. Med. **61**:860, 1938.
24. Pardee, H. E.: Clinical Aspects of the Electrocardiogram, ed. 4, New York, 1941, Paul B. Hoeber, Inc., p. 292.
25. Don, C. S., and Langley, G. J.: Some Aspects of the Electrocardiogram in Toxic Goiter, Quart. J. Med. **1**:9, 1932.
26. Bernstein, S. S.: Cardiac Arrythmias in Graves' Disease, J. Mt. Sinai Hosp. **1**:166, 1934.
27. Digilio, V.: Reversible Bundle Branch Block in a Case of Toxic Goiter, Am. Heart J. **15**:116, 1938.
28. Likoff, W. B., and Levine, S. A.: Thyrotoxicosis as the Sole Cause of Heart Failure, Am. J. M. Sc. **206**:425, 1943.
29. Lahey, F. H., Hurxthal, L. M., and Driscoll, R. E.: Thyrocardiac Disease, Ann. Surg. **118**:681, 1943.
30. Ernstene, A. C.: The Cardiovascular Complications of Hyperthyroidism, Am. J. M. Sc. **195**:248, 1938.
31. Andrus, E. C.: Heart Failure With Hyperthyroidism, New York State J. Med. **29**:661, 1929.
32. Hurxthal, L. M.: Heart Failure and Hyperthyroidism, Am. Heart J. **4**:103, 1928.
33. McPhedran, H.: Cardiovascular Changes in Toxic Goiter, Canad. M. A. J. **46**:471, 1942.
34. Maher, C. C., and Sittler, W. W.: The Cardiovascular State in Thyrotoxicosis, J. A. M. A. **106**:1546, 1936.
35. White, P. D.: Heart Disease, ed. 3, New York, 1944, The Macmillan Company, p. 412.
36. Lerman, J., and Means, J. H.: Cardiovascular Symptomatology in Exophthalmic Goiter, Am. Heart J. **8**:55, 1932.
37. Means, J. H.: The Thyroid and Its Diseases, Philadelphia, 1937, J. B. Lippincott Company, p. 322.

38. Hurxthal, L. M.: Auricular Fibrillation in Patients With Goiter, Am. J. M. Sc. **179:**507, 1930.
39. Slesinger, G. E.: Auricular Fibrillation and the Thyroid, Brit. M. J. **1:**65, 1939.
40. Haines, S. F., and Barnes, A. R.: Exophthalmic Goiter With Cardiac Decompensation and Normal Cardiac Rhythm. Case Report, Proc. Staff. Meet., Mayo Clin. **13:**142, 1938.
41. Anderson, J. P.: The Incidence of Auricular Fibrillation and Results of Quinidine Therapy, AM. HEART J. **8:**128, 1932.
42. Barker, P. S., Bohning, A. L., and Wilson, F. N.: Auricular Fibrillation in Graves' Disease, AM. HEART J. **8:**121, 1932.
43. Means, J. H.: The Thyroid and Its Diseases, Philadelphia, 1937, J. B. Lippincott Company, p. 449.
44. Segal, H. N., and Means, J. H.: The Immediate Effect of Subtotal Thyroidectomy in Toxic Goiter, Arch. Surg. **8:**176, 1924.

Announcement

Dr. Jonathan C. Meakins of Montreal, Canada, has accepted the Editorship of the American Heart Journal. The Journal will continue publication under his able leadership and with the assistance of an Advisory Council and with an Editorial Board to be announced in a later issue.

THE CONUS ARTERY: A THIRD CORONARY ARTERY

MONROE J. SCHLESINGER, M.D., PAUL M. ZOLL, M.D.,
AND STANFORD WESSLER, M.D.
BOSTON, MASS.

THE portion of the right ventricle in the human heart known as the area of the conus arteriosus often has a unique arterial blood supply through a vessel accessory to the two main coronary arteries. The supernumerary vessel in this region, which we have called the "conus artery," arises by a separate ostium behind the right aortic valve cusp, courses over the anterosuperior surface of the right ventricle, and terminates near the anterior interventricular groove. Significant relations were found between the anatomic variations of this coronary artery and the remainder of the coronary arterial tree and the myocardium.

LITERATURE

Supernumerary coronary arteries have been observed since the days of the early anatomists. Nevertheless, they receive little attention in most modern anatomic textbooks and are usually considered as uncommon variations of little significance.[1,2] Spalteholz[3] did not refer directly to this variation in his monograph. Grant[4] specifically stated that "the accessory coronary arteries spring from the aortic sinuses in about 4 per cent of hearts." Although Gross[5] also commented on their infrequency, he did mention the potential function of such vessels when occlusions develop in the main coronary arteries. Clinical treatises on coronary artery disease[6] make scant mention of these vessels. There is no reference to them in Abbott's discussion[7] of anomalies of the coronary arterial tree.

A few investigators have noted an especially high incidence of supplementary right coronary arteries. More than a century ago, the anatomist Richard Quain[8] clearly showed in the first plate of his atlas a large supplementary vessel arising near the right coronary artery. Quain's plates were based upon 930 dissections, and he stated that "the arteries are represented according to their most frequent arrangement."

In 1904 Banchi[9] injected 100 hearts through the aorta with a standard chalk mass. He reported that the first ventricular branch of the right coronary artery arose directly from the sinus of Valsalva in 33 per cent of human hearts, and found two such accessory arteries in 3 per cent of his series. Banchi stated that this vessel, which he called the "adipose artery," supplied the conus arteriosus and the superior portion of the sternocostal surface of the right ventricle.

From the Departments of Medicine and Pathology, Harvard Medical School, and the Medical Research and Pathology Laboratories, Beth Israel Hospital, Boston, Mass.

This study was aided by a grant from the Life Insurance Medical Research Fund.

On the basis of an injection study, Piquand[10] referred to the conus artery as "l'artère graisseuse de Vieussens" and stated that it was present in one-third of human hearts.

Utilizing the simple technique of unaided dissection, Symmers[11] determined the number of coronary arteries in 100 consecutive human hearts without regard to the presence of pathology. He found one or more accessory coronary arteries in 38 per cent. The diameters of these supplementary vessels were small (0.5 to 2.0 mm.), and they arose from the aorta within a few millimeters of the mouth of the right coronary artery. Symmers was unable to trace them farther than 6.0 to 8.0 cm. over the anterior aspect of the right ventricle, so that he did not establish their final course and distribution.

Again, in 1922 Crainicianu[12] injected 200 human hearts with radiopaque mass and found a vessel which he called the "arteria praeinfundibularis" arising in 45 per cent of the series by a separate mouth 1.0 to 3.0 mm. in diameter. In his opinion, the origin of this vessel from the aorta was only an unimportant anatomic variation of no significance in the nutrition of the heart.

Investigations in a diverse group of animals have revealed variations in the number of coronary arteries arising directly from the aorta. Fish have two, amphibia have one, and reptiles have one or two, but all show variations in number.[13] Among mammals the usual number is two. In the dog and pig this is relatively constant: among such animal hearts injected in our laboratory,[14] only ten dog hearts among ninety, and one pig heart of seventy-nine showed an accessory right coronary artery.

The origins of the coronary arteries in primates were investigated by Chase.[15] There were two coronary arteries in over one-half of the hearts of 266 rhesus monkeys: in 38 per cent of his series an accessory vessel arose from the aortic sinus by a common mouth with the right coronary; in approximately 6 per cent, a third vessel arose by a separate mouth near the right coronary ostium. Chase and De Garis[16] extended these observations to include other higher primates and found twenty-three accessory arteries in the coronary trees of thirty-six hearts. In only one of these hearts was there also a supplementary coronary artery on the left. The findings in the literature and in our series are tabulated below (Table I).

TABLE I. INCIDENCE OF CONUS ARTERY

ANIMAL	NUMBER OF HEARTS STUDIED	HEARTS WITH CONUS ARTERY		REFERENCE
		NUMBER	PER CENT	
Dog	90	10	11	Schlesinger[14]
Pig	79	1	1	Schlesinger[14]
Rhesus monkey	266	17	6	Chase[15]
Higher primates	36	23	65	Chase and De Garis[16]
Man	100	33	33	Banchi[9]
	—	—	33	Piquand[10]
	100	38	38	Symmers[11]
	200	—	45	Crainicianu[12]
	651	332	51	Present series

METHOD AND MATERIALS

The human hearts on which our observations are based were all prepared by the method of injection plus dissection previously reported.[17] Briefly, this consists of (1) injecting a radiopaque lead-agar mass of different colors into the two main coronary arteries, (2) unrolling the heart so that its entire arterial tree lies in one plane, (3) taking a roentgenogram of the unrolled heart, and (4) carefully dissecting the coronary arteries, using the film as a guide. This technique discloses the narrowings, occlusions, and anastomoses in the visualized coronary arteries in every heart. The conus artery attracted our attention in routine injections by this method, when the injection mass occasionally filled the conus artery by anastomotic pathways and leaked through its mouth into the aorta. Of a total series of 1,000 hearts, only 651 were used in the present analysis. The others were rejected because the observations on the conus artery were incomplete.

OBSERVATIONS

1. *Anatomy of Conus Artery.*—The conus artery, a supernumerary to the right coronary artery, arises by a separate ostium in the aorta and sends branches to the area of the conus arteriosus. It courses in the epicardium over the anterosuperior aspect of the right ventricle and terminates in small arterial twigs near the anterior interventricular groove. The film of the unrolled heart (Fig. 1) shows the close proximity of the branches of the conus artery to the branches of the left descending coronary artery. The conus artery usually arises close to the ostium of the right coronary artery, behind the same semilunar aortic cusp. The vessel varies considerably in size; although usually small (0.4 to 1.0 mm. in internal diameter at its origin), it may reach a diameter of 2.0 mm. or more (Fig. 2).

When the conus artery is not present, the area of the conus arteriosus is supplied by the first ventricular branch of the right coronary artery (Fig. 3). This first branch of the right coronary artery, in all respects similar to the conus artery except for its point of origin, was also given special study for purposes of comparison.

2. *Incidence of Conus Artery.*—In one-half of the 651 human hearts, single or multiple conus arteries were present (Table II). The occurrence of conus arteries is unrelated to age or sex (Table III, *A* and *B*).

TABLE II. ORIGIN OF ARTERY TO CONUS ARTERIOSUS (651 HEARTS)

	NUMBER OF HEARTS		PERCENTAGE	
Conus Artery	332		51	
Single aortic mouth		319		49
Multiple aortic mouths		13		2
First ventricular branch of right coronary artery	319		49	

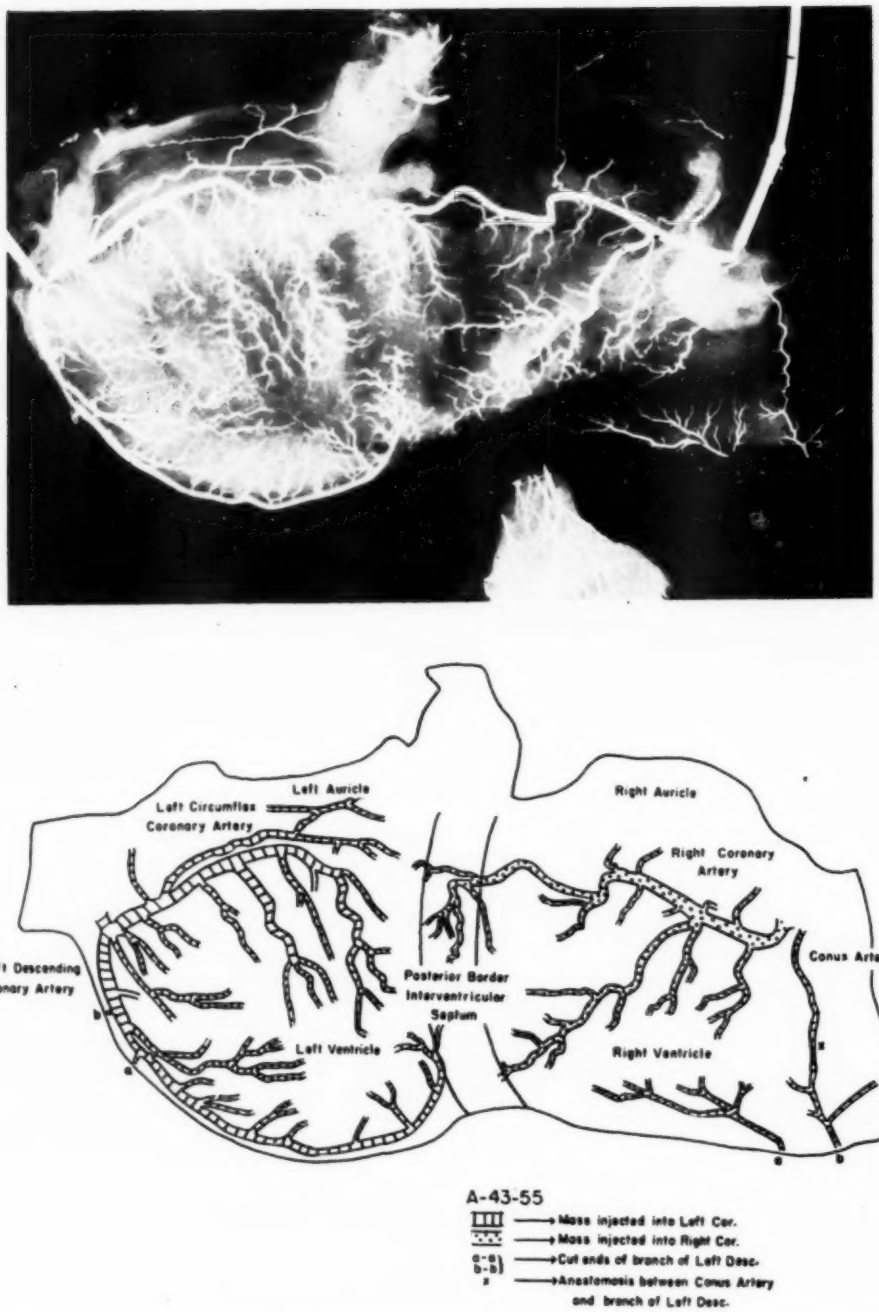
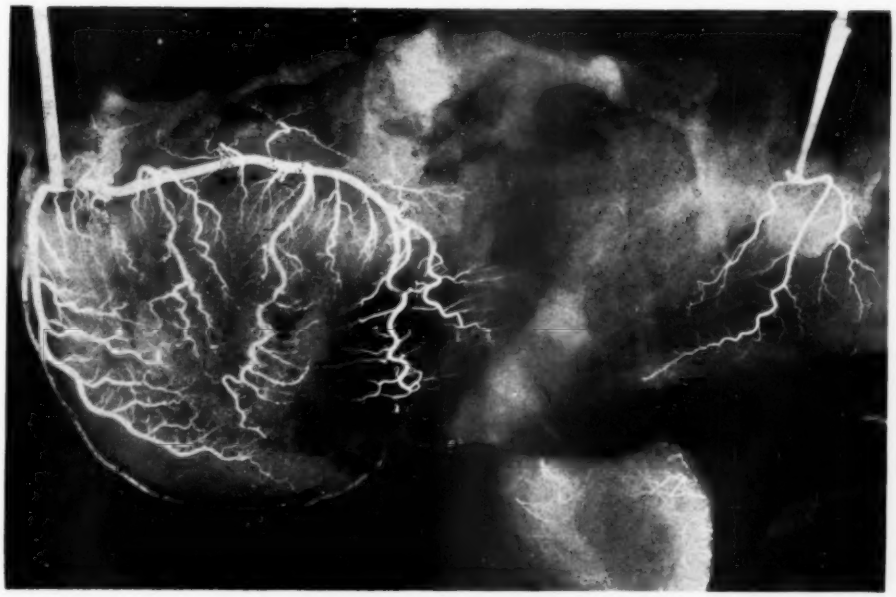


Fig. 1.—X-ray and diagram of injected normal heart showing conus artery in relation to other coronary arteries.

Case A43-55. A 59-year-old man, without evidence of hypertension, angina pectoris, or congestive failure, who died from carcinoma of the lung. Heart weight, 308 grams. No hypertrophy, valvular disease, coronary artery narrowing, or myocardial fibrosis was found. Anastomosis of the left descending coronary artery with the conus artery was present.



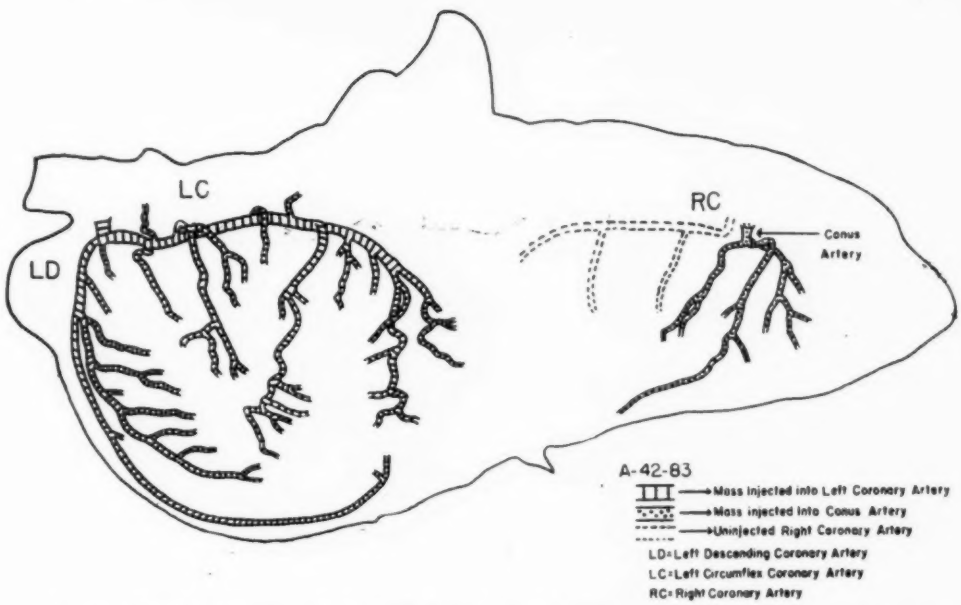
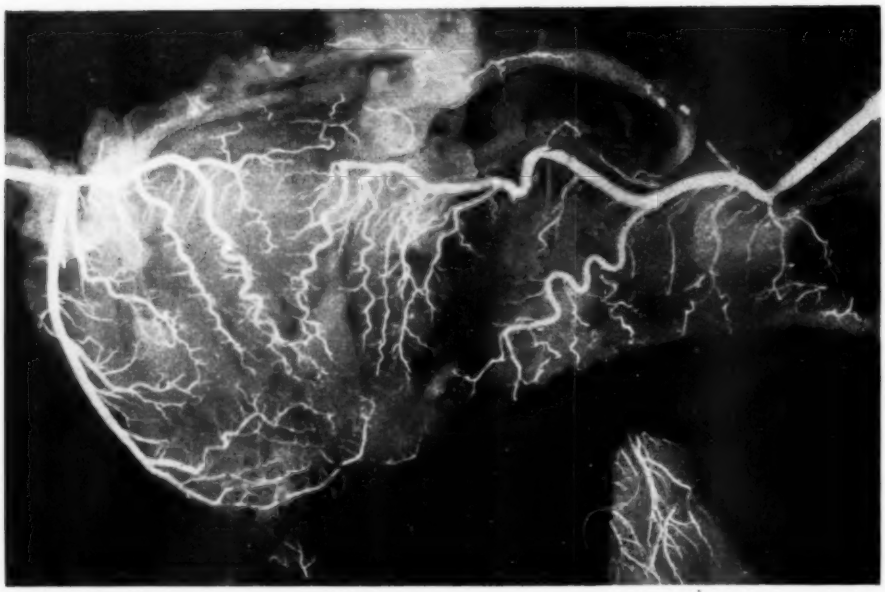


Fig. 2.—X-ray and diagram of injected normal heart showing large conus artery cannulated and injected with mass.

Case A42-83. A 56-year-old man without hypertension, angina pectoris, or congestive failure who died from carcinoma of the colon. Heart weight, 330 grams. No hypertrophy, valvular disease, coronary arterial narrowing, myocardial fibrosis, or anastomoses were found.



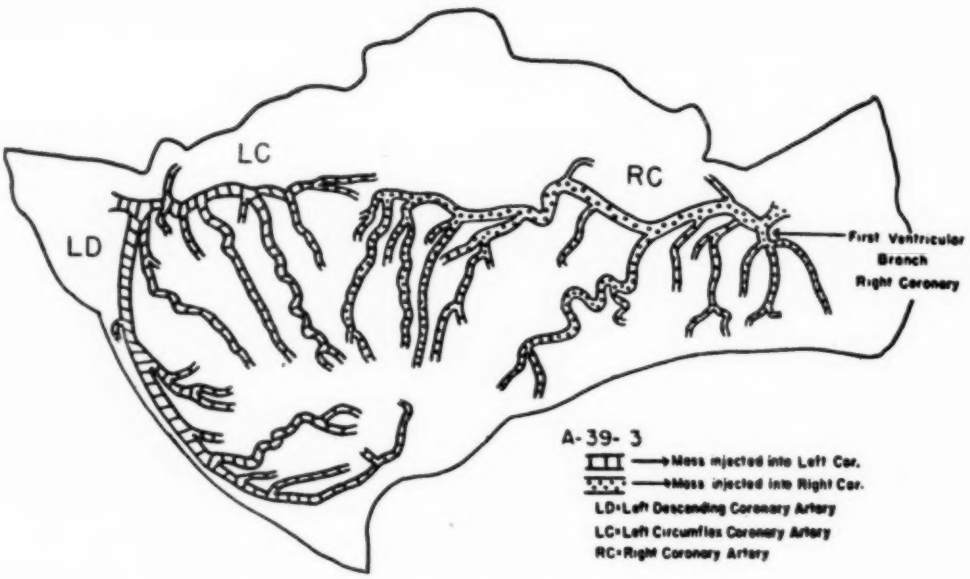


Fig. 3.—X-ray and diagram of injected normal heart showing area of conus arteriosus supplied by homologue of conus artery, the first ventricular branch of the right coronary artery.

Case A39-3. A 56-year-old man, who died from lobar pneumonia. No hypertension, angina pectoris, or congestive failure was present. Heart weight, 250 grams. No hypertrophy, valvular disease, coronary artery narrowing, myocardial fibrosis, or anastomoses were found.

TABLE III, A. ORIGIN OF ARTERY TO CONUS ARTERIOSUS IN RELATION TO AGE

AGE IN YEARS	NUMBER OF HEARTS				
	0–19	20–39	40–59	60–	TOTAL
Conus artery	11 (46%)	48 (59%)	118 (50%)	155 (50%)	332 (51%)
First ventricular branch right coronary artery	13	33	117	156	319
Totals	24	81	235	311	651

TABLE III, B. ORIGIN OF ARTERY TO CONUS ARTERIOSUS IN RELATION TO SEX

	NUMBER OF HEARTS	
	MEN	WOMEN
Conus artery	207 (53%)	125 (48%)
First ventricular branch right coronary artery	185	134
Totals	392	259

The high incidence of supernumerary conus arteries on the right is in marked contrast to the rare occurrence of vessels accessory to the left coronary artery system. The length of the common left coronary artery trunk, however, is quite variable; indeed, it is occasionally so short that the left descending and left circumflex coronary arteries arise from a common ostium in the aorta. In only four instances in the 1,000 injected hearts was the common left coronary artery stem absent completely, so that the left descending and left circumflex coronary arteries arose by separate mouths from the aorta. In two of these four hearts, the separate left circumflex coronary ostium was misplaced, arising from the aorta behind the same cusp as the right coronary artery. Complete separation of the mouths of the two left coronary arteries is apparently a major congenital anomaly.

3. *Occlusions in the Conus Artery.*—In a previous communication based on 400 hearts,[18] the incidence and localization of occlusions in the main coronary arteries and their branches were reported. Detailed study of the occlusions in the branches of the coronary arteries was deferred, however, pending the accumulation of a larger series, because the variability in the number, origin, and distribution of such branches makes difficult any generalizations about them.

The conus artery and its homologue, the first ventricular branch of the right coronary, are distinct, have a relatively constant distribution, and differ only in origin. They lend themselves, therefore, to a comparative study of

the incidence of occlusions in two constant vessels of the coronary arterial tree. In the 651 hearts studied, occlusions were found in only six (1.8 per cent) of the 332 conus arteries and in five (1.6 per cent) of the 319 homologous right coronary arterial branches (Table IV). The incidence of occlusions in the conus artery and its homologue was compared with the incidence in the first branch of the left descending (2.0 per cent) and of the left circumflex (0.9 per cent) coronary arteries (Table V). In addition, all the "primary branches"* of the left decending and left circumflex coronary arteries were studied in the same way. All primary branches which measured over 1.0 mm. in diameter on the roentgenograms of the injected hearts were counted, and the incidence of occlusions in them was determined. In 976 hearts in which adequate data of this nature were available, ninety occlusions (1.5 per cent) were present in the 5,846 primary branches of the left descending coronary artery and seventy-two occlusions (1.5 per cent) were found in the 4,880 primary branches of the left circumflex coronary artery.

TABLE IV. INCIDENCE OF OCCLUSIONS IN CONUS ARTERY AND IN FIRST VENTRICULAR BRANCH OF RIGHT CORONARY ARTERY

VESSEL	NO. OF VESSELS	NO. OF OCCLUSIONS	PER CENT OF VESSELS WITH OCCLUSIONS
Conus artery	332	6	1.8
First ventricular branch right coronary artery	319	5	1.6

TABLE V. INCIDENCE OF OCCLUSIONS IN BRANCHES OF LEFT DESCENDING AND LEFT CIRCUMFLEX CORONARY ARTERIES

VESSEL	NO. OF VESSELS	NO. OF OCCLUSIONS	PER CENT OF VESSELS WITH OCCLUSIONS
First branch of left descending artery	976	20	2.0
First branch of left circumflex artery	976	9	0.9
All branches of left descending artery	5,846	90	1.5
All branches of left circumflex artery	4,880	72	1.5

The incidence of occlusions is of the same order of magnitude in the conus artery (1.8 per cent); in the first branches of the left descending (2.0 per cent), left circumflex (0.9 per cent), and right coronary (1.6 per cent) arteries; and in all other primary branches (1.5 per cent). The incidence of occlusions in all the primary branches is much less than that previously reported[18] in the main coronary arteries, and is one quarter of that in the first 4.0 cm. of the main stems of the coronary arteries, and one half of that in the distal segments of the main stems.

*By "primary branch" is meant any artery arising directly from the left descending, left circumflex, or right coronary artery.

4. *Anastomoses With Conus Artery.*—In this series, anastomotic communications between coronary arteries are demonstrated either by the injection of a vessel distal to a complete occlusion or by a mixture of colors in nonoccluded vessels. The distribution of colors permits identification of the source of the injected mass and the pathways of anastomoses. Nondissectible, submacroscopic anastomoses between two primary branches of a nonoccluded artery are not noticed by this method, since they are filled with mass of the same color. Therefore, in hearts without occlusions, anastomoses between the first ventricular branch of the right coronary artery and the remainder of the right coronary artery would not be detected.

On the other hand, full information regarding anastomoses to the conus artery is obtainable because this artery has a separate uncannulated mouth in the aorta. Anastomotic connections between conus arteries and the injected coronary arterial tree are completely demonstrated whether or not the conus artery is occluded, for it can be filled with mass only by way of anastomotic pathways. The conus artery is strategically placed between the branches of the left descending coronary artery and the right coronary artery. It is a potential path of anastomosis to either of these major vessels. The conus artery thus offers a unique opportunity for a complete study of anastomotic filling of a single coronary vessel.

Anastomotic filling of the conus artery was observed in 123 of the 332 hearts with conus arteries. No correlation was found between the age of the patient and the incidence of anastomosis with this vessel (Table VI).

TABLE VI. INCIDENCE OF ANASTOMOSES WITH CONUS ARTERY IN RELATION TO AGE

	NUMBER OF HEARTS				
AGE IN YEARS	0–19	20–39	40–59	60–	TOTAL
Nonanastomotic conus artery	8	31	70	100	209
Anastomotic conus artery	3 (22%)	17 (35%)	48 (41%)	55 (35%)	123 (37%)
Totals	11	48	118	155	332

From the 332 hearts with conus arteries, there was selected a group of 141 hearts which did not exhibit narrowings or occlusions of the coronary arteries, or any valvular disease. Hearts with hypertrophy were not excluded from this selected "control group." Anastomotic filling was found in the conus arteries of thirty-one (22 per cent) of these 140 selected control hearts (Table VII). In the same group of control hearts, twenty-six (18 per cent) showed interarterial anastomoses with vessels other than the conus artery. Although these figures are statistically similar, the incidence of anastomoses in conus arteries is signifi

cant, because the remainder of the coronary arterial tree presents several times as large a potential bed for anastomoses as that surrounding the conus artery.

TABLE VII. RELATION OF CONUS ARTERY ANASTOMOSES TO CORONARY ARTERY OCCLUSION

	141 HEARTS WITHOUT CORONARY ARTERY NARROWING, OCCLUSION, OR VALVULAR DISEASE		71 HEARTS WITH OLD OCCLUSION	
	NO. OF HEARTS	PER CENT	NO. OF HEARTS	PER CENT
Anastomoses with conus artery	31	22	43	61
Anastomoses elsewhere in entire coronary arterial tree	26	18	70	100

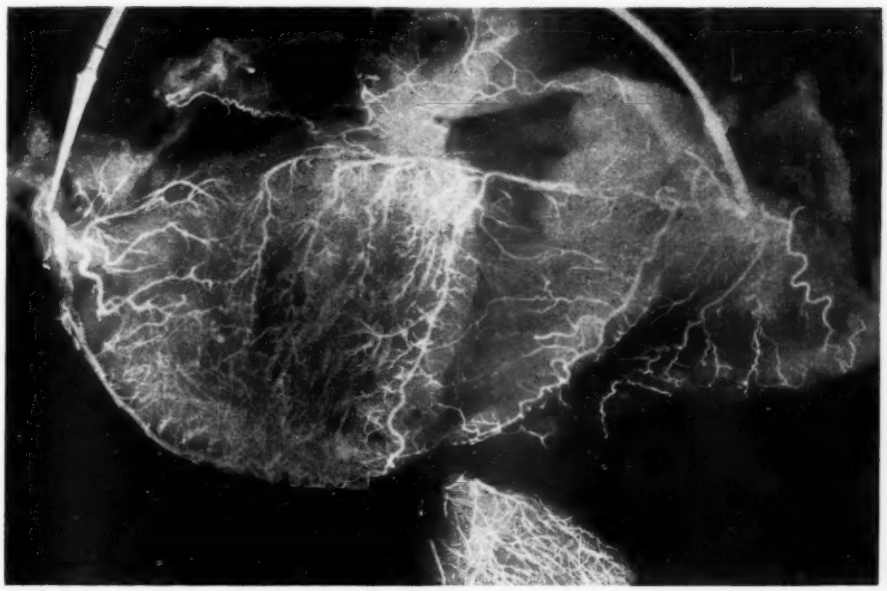
The potentialities of the conus artery as a source of anastomotic blood supply to the myocardium are more fully displayed in the hearts with old coronary artery occlusions. Among the 332 injected hearts with conus arteries, there were seventy-one with old occlusions in vessels other than the conus artery. There was anastomotic filling of forty-three (61 per cent) of the conus arteries of these hearts (Table VII). In keeping with previous observations,[18] almost universal (99 per cent) anastomotic filling was found in vessels distal to old occlusions (Table VII).

Thus, there was an increase in the incidence of anastomoses involving the conus artery, from 22 per cent in hearts without coronary artery or valvular disease to 61 per cent in hearts with old coronary artery occlusions. Occlusions anywhere in the coronary arterial system appear to stimulate anastomotic channels between the conus vessel, which receives blood directly from the aorta, and other coronary artery branches not so situated.

ILLUSTRATIVE CASES

Indeed, in individual hearts it was often obvious that conus arteries were important anastomotic channels for the transport of blood directly from the aorta to a portion of the coronary arterial tree distal to an occlusion. The value of such anastomotic connections depends upon their number and caliber, the size of the conus artery, and also upon the location of the anastomosis in relation to the narrowings or occlusions. The following two cases serve to illustrate these potentialities of the conus artery.

CASE 1 (A42-85).—Fig. 4 represents a heart in which the conus artery was a major source of blood supply to the other coronary arteries distal to occlusions within them. This patient had had angina pectoris for three years, without clinical evidence of myocardial infarction. Although five old occlusions were found in the three main coronary arteries, there was no old or fresh infarction in this heart. During life a considerable portion of the blood supply to the myocardium was probably derived from the unobstructed conus artery. This vessel, of appreciable size, helped prevent myocardial infarction by supplying blood through a series of anastomotic pathways.



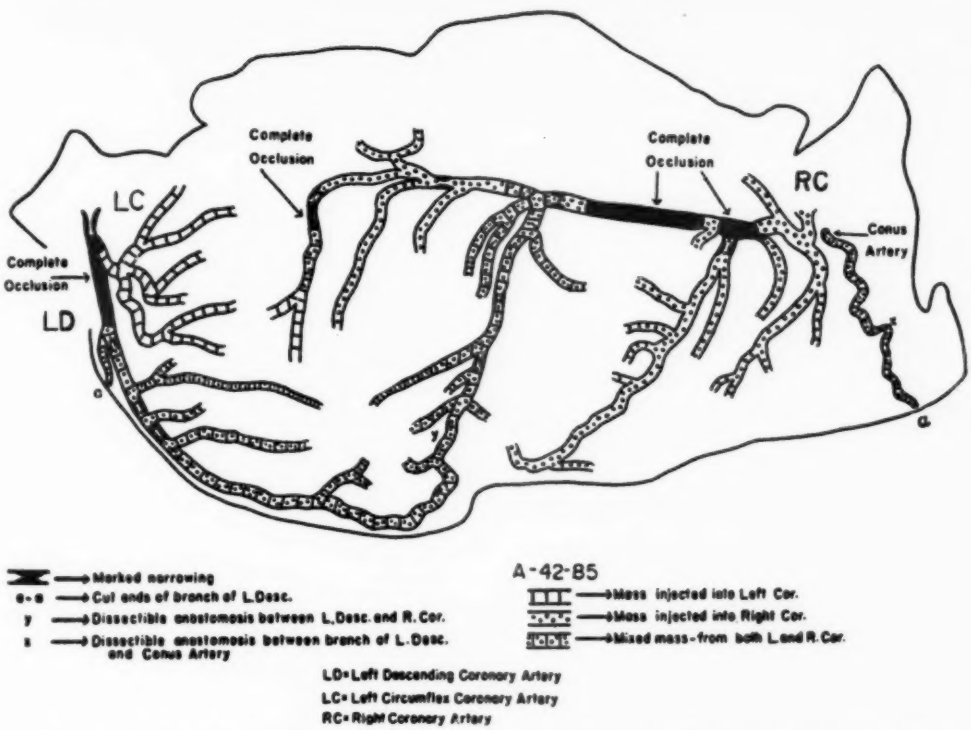


Fig. 4.—X-ray and diagram of injected heart showing occlusions in all main coronary arteries, with anastomosis between branch of left descending and conus arteries.

Case A42-85. A 60-year-old hypertensive man, whose death from pyelitis was preceded for three years by angina pectoris and exertional dyspnea. Heart weight, 500 grams. Left ventricular hypertrophy. Five old occlusions in left descending, left circumflex, and right coronary arteries. Moderate myocardial fibrosis without myocardial infarction. Extensive anastomosis between left descending and right coronary arteries, as well as large, grossly dissectible anastomosis between conus artery and branch of left descending artery distal to an occlusion in the latter.

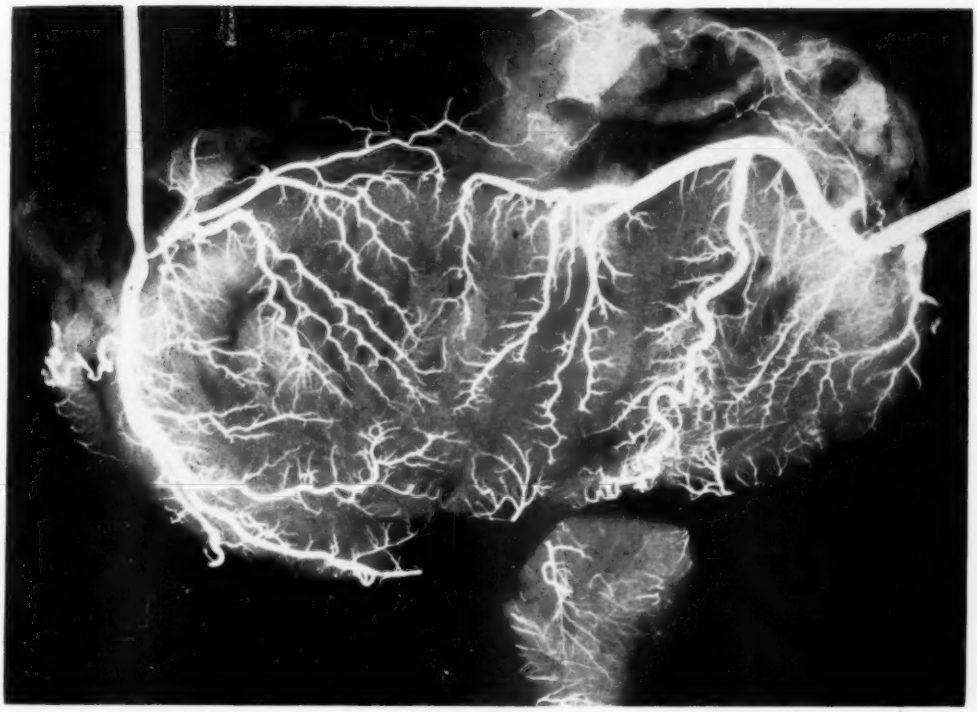
CASE 2 (A46-60).—Fig. 5 represents a heart with congenital pulmonic stenosis in which the conus artery and the left descending coronary artery together brought a real, though perhaps insignificant, amount of aortic blood to the pulmonary artery distal to the stenosis. The anastomotic circulation in this heart presents a spontaneous systemic-pulmonic shunt analogous to those now being produced surgically for the treatment of pulmonic stenosis.

DISCUSSION

The artery to the conus arteriosus (conus artery), arising directly from the aorta by an independent ostium in 50 per cent of human hearts, has not received the attention it deserves. Although study of this vessel by ordinary dissection is comparatively easy, it is facilitated by the use of an injection method. Thus, there are obtained, in a variety of hearts, additional data which would not be available without such a technique. This method, which was especially devised for studying arterial occlusions, disclosed an incidence of occlusions in the conus artery similar to that in the primary branches of the coronary arterial tree. Although the conus artery arises directly from the aorta, it does not have the high incidence of occlusions found in the first 4 cm. of the coronary artery trunks. Our observations, therefore, lend no support to the concept that the higher incidence of occlusions near the ostia of the main coronary arteries is, in some way, related to the presumably higher blood pressure in this portion of these vessels.

Since the conus artery receives blood directly from the aorta, it differs markedly as a potential collateral source of blood supply from its homologue, the first ventricular branch of the right coronary artery. Because of its separate origin, the conus artery is independent of obstruction so often found at or near the mouth of the right coronary artery, and affecting its first ventricular branch.[18] By the special features which distinguish it from the rest of the coronary arterial tree, the conus artery appears particularly suited as a collateral source of blood supply. Its direct communication with the aorta and its location between the main left descending and the right coronary arteries make it a ready source of anastomotic connection between the aorta and the coronary arterial tree distal to the zones in which the incidence of occlusions is highest. Furthermore, the low incidence of occlusions in the conus artery, lower than in any other coronary artery directly connected with the aorta, enhances its value as an effective pathway of collateral blood supply. In the presence of old occlusions anywhere in the heart, the incidence of anastomoses with the conus artery increases threefold. This unique vessel responds to the need for increased blood supply as if it were an accessory artery strategically placed between the left descending and right coronary arteries, which supply most of the blood in most human hearts. It appears that the clinical consequences of occlusion in these two coronary arteries may be significantly influenced by the presence or absence of a conus artery.

The existence of this supernumerary coronary artery, with potential anastomosis to the other coronary vessels, has not always been considered in experiments on coronary flow. In such experiments, its presence or absence should be specifically determined, and methods should be specifically devised for pre-



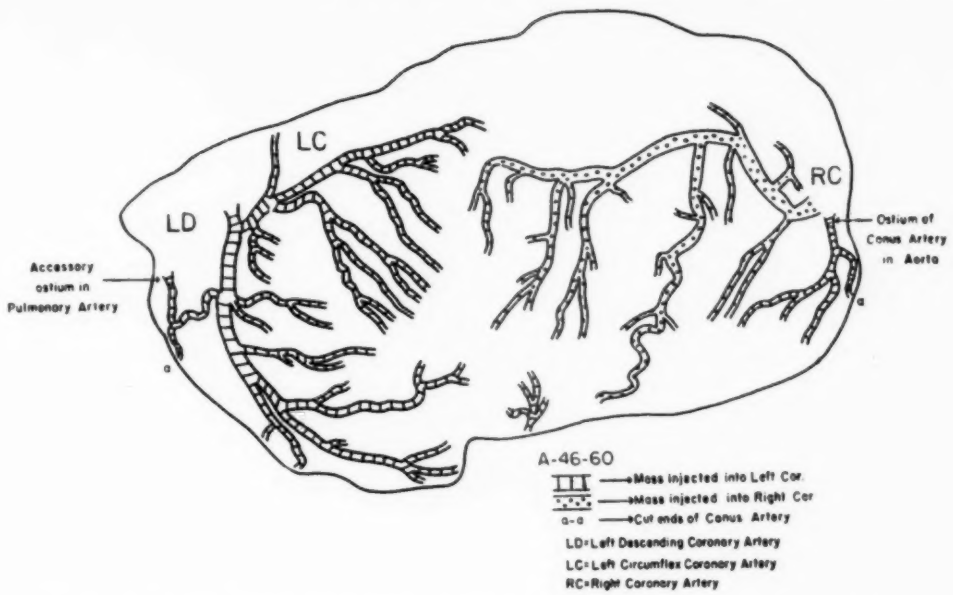


Fig. 5.—X-ray and diagram of injected heart with pulmonic stenosis, showing anastomosis between aorta and pulmonary artery via left descending coronary and conus arteries.

Case 46-60. A 49-year-old woman, who died of chronic leucemia. Enlarged heart with a pulmonic systolic murmur and thrill. No hypertension, angina pectoris, or congestive failure was noted. Heart weight, 445 grams. Right ventricular hypertrophy; interauricular septal defect; congenital, quadricuspid pulmonic stenosis. No coronary artery narrowing or myocardial fibrosis. Grossly dissectible anastomosis between the conus artery and the left descending coronary artery, with additional mouth in pulmonary artery distal to the pulmonic stenosis.

venting flow through this vessel from irrigating the coronary tree or from being confused with flow from the chambers of the heart.

CONCLUSIONS

1. In 50 per cent of the 651 human hearts studied, the conus arteriosus is normally supplied by an artery, the conus artery, which is not a branch of the right or left coronary artery, but arises directly from the aorta.

2. The incidence of occlusions in the conus artery is much lower than in the three main coronary artery trunks, but is similar to that in the primary branches of the coronary arterial tree.

3. The conus artery often serves as a source of anastomotic blood supply directly from the aorta to the other vessels of the heart when these are narrowed or occluded.

4. The amount of myocardial damage resulting from coronary artery occlusion and narrowing is in part determined by the presence or absence of anastomoses between the conus artery and the rest of the coronary arterial tree.

REFERENCES

1. Gray, H.: Anatomy of the Human Body, ed. 24, Philadelphia, 1942, Lea & Febiger, p. 549.
2. Cunningham's Textbook of Anatomy, ed. 8, New York, 1943, Oxford University Press, p. 1207.
3. Spalteholz, W.: Die Arterien der Herzwand, Leipzig, 1924, S. Hirzel.
4. Grant, J. C. B.: A Method of Anatomy, ed. 3, Baltimore, 1944, Williams & Wilkins Company, p. 520.
5. Gross, L.: The Blood Supply to the Heart, New York, 1921, Paul B. Hoeber, Inc., p. 30.
6. Wearn, J. T.: "The Anatomy of the Coronary Vessels," In: Levy, R. L.: Diseases of the Coronary Arteries and Cardiac Pain, New York, 1936, The Macmillan Company, pp. 33-34.
7. Abbott, M. E.: Congenital Heart Disease, Nelson Loose-Leaf Medicine **4**:260, 1932.
8. Quain, R.: Anatomy of the Arteries (Atlas), Plate I, London, 1844, Taylor & Walton.
9. Banchi, A.: Morfologia delle arteriae coronariae cordis, Arch. ital. di anat. e di embriol. **3**:87, 1904.
10. Piquand, G.: Recherches sur l'Anatomie des Vaisseaux Sanguins du Cour, J. de l'Anat. et de la Physiol. **46**:310, 1910.
11. Symmers, W. St. Clair: Note on Accessory Coronary Arteries, J. Anat. & Physiol. **41**:141, 1907.
12. Crainicianu, A.: Anatomische Studien über die Coronararterien und Experimentelle Untersuchungen über Ihre Durchlässigkeit, Virchow's Arch. f. Path. Anat. **238**:1, 1922.
13. Grant, R. T., and Regnier, M.: The Comparative Anatomy of the Cardiac Coronary Arteries, Heart **13**:285, 1926.
14. Schlesinger, M. J., and Zoll, P. M.: Unpublished data.
15. Chase, R. E.: The Coronary Arteries in 266 Hearts of Rhesus Monkey, Am. J. Phys. Anthropol. **23**:299, 1938.
16. Chase, R. E., and De Garis, C. F.: Arteriae Coronariae (Cordis) in the Higher Primates, Am. J. Phys. Anthropol. **24**:427, 1939.
17. Schlesinger, M. J.: An Injection Plus Dissection Study of Coronary Artery Occlusions and Anastomoses, AM. HEART J. **15**:528, 1938.
18. Schlesinger, M. J., and Zoll, P. M.: Incidence and Localization of Coronary Artery Occlusions, Arch. Path. **32**:178, 1941.

VI. CORRELATION OF ELECTROCARDIOGRAPHIC AND PATHOLOGIC FINDINGS IN POSTEROLATERAL INFARCTION

GORDON B. MYERS, M.D., HOWARD A. KLEIN, M.D., AND TOMIHARU HIRATZKA, M.D.
DETROIT, MICH.

WILSON and co-workers[1,2] have drawn attention to the electrocardiographic findings in posterolateral infarction, as distinguished from plain posterior and high lateral infarction. Their descriptions cover the classical findings in the standard leads and in unipolar thoracic, esophageal, and limb leads. Typical cases are manifested by abnormal Q_2T_2 and Q_3T_3 patterns due to the posterior lesion, accompanied by a small Q_1 and inverted T_1 due to the lateral lesion.[1,2,3] However, even the full pattern in the standard leads cannot be regarded as pathognomonic of posterolateral infarction, since it may be duplicated by anteroposterior infarction[4] and perhaps by anterolateral infarction when the heart is in vertical position.[1,5]

Valuable additional information would be expected from the use of multiple unipolar leads, since Leads V_5, V_6, and aV_L reveal many lateral lesions not diagnosable from Lead I,[1,2,6] whereas Lead aV_F provides a more reliable index of the posterior lesion than do Leads II and III.[7,8] The typical findings, as set forth by the Wilson group,[1,2] are: (1) abnormal Q waves in the unipolar leads from the left leg and the ventricular levels of the esophagus; (2) diagnostic QT patterns in Lead V_6 and perhaps in Lead V_5, as well; and (3) reciprocal changes in leads from the right side of the precordium, consisting of early depression of the RS-T segment and subsequent exaggeration of the R and T waves.

No data are available as to the accuracy which may be attained in the detection and localization of posterolateral infarcts through the use of multiple unipolar leads, since the Wilson group has had little opportunity to follow their patients to autopsy, whereas other workers have not given consideration to posterolateral infarction as a separate entity. Therefore, an analysis will be presented of the electrocardiographic findings in our group of thirty-three patients with pathologic evidence of infarction of the posterolateral wall of the left ventricle. Fourteen of these will be presented in detail; eleven others were reported previously[8]; and the eight remaining will appear in a succeeding manuscript on primary lateral infarction.[9] The findings pertaining to the lesion of the posterolateral wall will be summarized for all cases.

From the Departments of Medicine and Pathology of Wayne University College of Medicine, and City of Detroit Receiving Hospital.

CASE REPORTS

CASE 124.—A 55-year-old diabetic woman gave a classical history of angina pectoris, beginning in January, 1945. The first prolonged attack of retrosternal constriction occurred on Dec. 25, 1945, and a second began on Jan. 13, 1946, leading to admission to the hospital the following day. In spite of strict bed rest, there were many recurrences of retrosternal pain, generally relieved by nitroglycerine. On February 19 a much more severe attack occurred, complicated by circulatory collapse. Blood pressure remained at shock levels until her death on February 25. No cardiac glycosides were given.

Electrocardiographic Findings.—Electrocardiograms reproduced in Fig. 1 include a tracing on March 6, 1945, approximately two months after the onset of the angina pectoris; a tracing on Jan. 15, 1946, twenty-four hours after admission; and a third on Feb. 19, 1946, two hours after the onset of the recurrent attack, which was complicated by shock and ended in death. The standard and precordial leads of the first tracing were considered within normal limits. Lead aV_L displayed a low upright P wave and a Q wave 1.0 mm. in depth and approximately 20 per cent of the amplitude of the succeeding slurred R wave. The RS-T junction was isoelectric, but the T wave was diphasic. This pattern could be within normal limits if transmitted from the

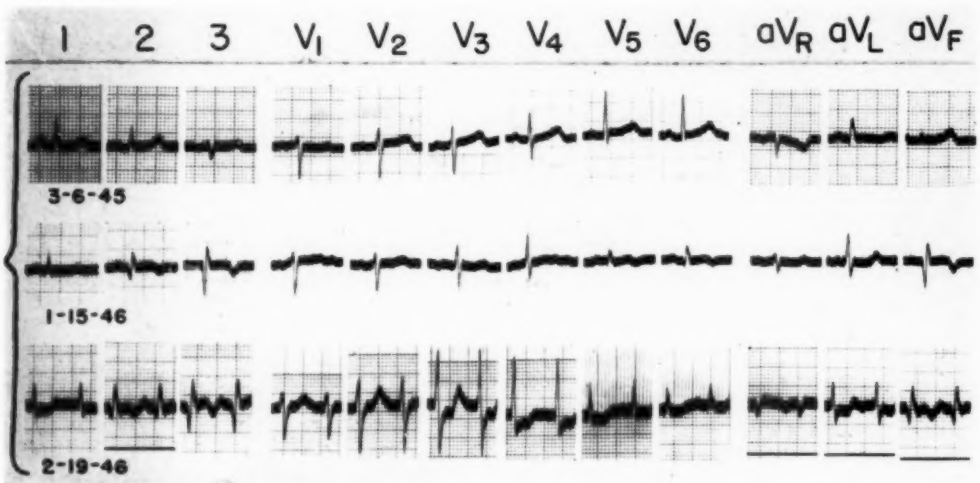


Fig. 1.—Electrocardiograms in Case 124 before and after the development of a posterolateral infarction.

posterobasal aspect of the left ventricle, but would have been abnormal if derived from the anterolateral wall of the left ventricle. In the latter event, such a finding could have been the result of left ventricular hypertrophy or of a small subendocardial lateral infarct. High precordial and axillary leads were indicated to settle the diagnosis, but unfortunately were not obtained because the patient did not return for observation in the outpatient department. The small, splintered R wave in Lead aV_F on March 6, 1945, was within normal limits. On Jan. 15, 1946, this was replaced by an abnormal QR complex and a cove-shaped inversion of the T wave typical of recent posterior infarction. The QRS complex in the first four precordial leads was almost identical with that recorded ten months previously, but the QRS complex in Leads V_5 and V_6 showed a significant change, characterized by the appearance of a Q wave and by a 66 per cent reduction in the voltage of the R wave. The QR complexes of Leads V_5 and V_6 were abnormal and, along with the bowing of the RS-T segment and inversion of the T wave, indicated continuation of the posterior infarct into the lateral aspect of the left ventricle. The standard leads were typical of posterior infarction, but failed to show the lateral extension. This was apparently due to reference of the potential variations of the uninfarcted anteroseptal wall of the left ventricle to the left arm, as indicated by

the similarity in the QRS complexes of Leads V_4 and aV_L. In serial tracings during the next month, the main change consisted in a doubling of the amplitude of the R wave in Leads V_1 through V_3, coupled with an increase in the height of the T wave in these leads to 4.0 to 5.0 millimeters. This was considered reciprocal to the organization of a posterolateral infarct. Comparison of the tracing of February 19 with the one taken the preceding day showed no significant change in the QRS pattern in any lead. The RS-T segment in Leads aV_F, II, and III showed increased upward bowing. The RS-T junction, which had been isoelectric in the precordial leads and in aV_L, became acutely depressed in Leads V_3, V_4, and aV_L and slightly depressed in Leads V_5 and V_6. Two alternative explanations were considered for the RS-T depression; namely, extension of the infarct subendocardially into the anterolateral wall of the left ventricle, and a reciprocal effect from reinfarction of the posteroseptal wall. The latter was favored because of the increased upward bowing of the RS-T segment in Lead aV_F.

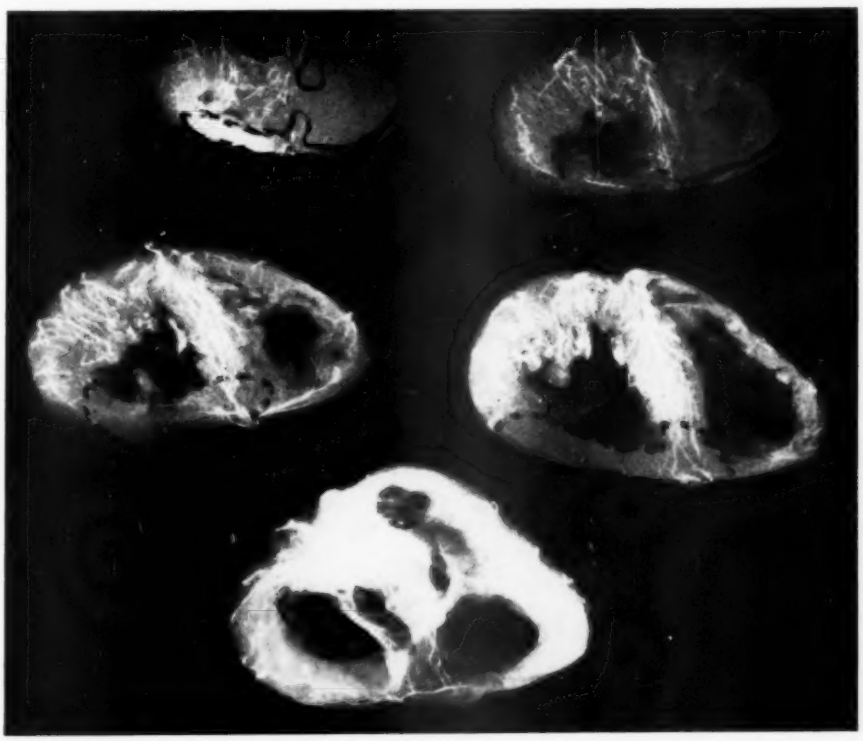


Fig. 2.—Roentgenogram of the injected heart in Case 124, showing an organizing posterolateral infarction in broken outline and a terminal posteroseptal and right ventricular infarct in solid lines.

Pathologic Findings.—The heart weighed 282 grams and exhibited an organizing transmural infarct of the entire posterior wall, as demarcated by the broken lines of Fig. 2. This infarct readily explained the abnormal QR pattern of Leads aV_F, II, and III on January 15. It extended into the posterolateral wall sufficiently to account for the abnormal QR pattern in Lead V_6 and the reciprocal increase in the upright deflections in Leads V_1 through V_3, but did not extend far enough forward to explain satisfactorily the findings in Lead V_5. Counterclockwise rotation or anterior displacement of the apex may have accounted for the transmission of the potential variations of the infarcted area to the anterior axillary line. There was microscopic evidence of recent reinfarction of the posterior wall of the left ventricle at its junction with the interventricular septum, together with an infarct of one week's duration in the apex of the right ventricle, as demarcated by the solid lines of Fig. 2. A large mural thrombus filled the entire apex

of the right ventricle. The anterior and anterolateral walls of the left ventricle were intact. Therefore, the acute RS-T depression in Leads V_2 through V_6 and in aV_L on February 19 represented a reciprocal manifestation of the extension into the posteroseptal wall of the left ventricle and/or the right ventricular infarct. Because of the absence of direct evidence of the latter in right ventricular Leads V_1 and V_2, it is probable that the reciprocal changes in left ventricular leads were referable exclusively to the extension into the posteroseptal wall of the left ventricle. The similarity of the QRS-T pattern in Leads V_1 and V_2 on February 19 to that in the same leads taken on the preceding day suggested that the right ventricular portion of the infarct may have developed after the tracing of February 19 had been taken. It is regrettable that no further electrocardiograms were obtained.

CASE 125.—A 50-year-old woman had had diabetes mellitus for twenty years, but was otherwise in good health until January, 1945, when she began to have transient attacks of retrosternal oppression, precipitated by exercise and relieved promptly by rest. Following the removal of a nontoxic thyroid adenoma in March, 1946, the angina disappeared for three months and then recurred with increasing severity. On Dec. 29, 1946, she was seized with a much more severe retrosternal pain, which continued unabated during the twenty-two hours intervening before hospitalization. She was admitted in profound circulatory collapse and died six hours later. No cardiac glycosides were administered.

Electrocardiographic Findings.—Electrocardiograms reproduced in Fig. 3 were taken at intervals during observation in the outpatient department and on the final admission five hours before death. The initial phase of the QRS complex was upright in the three precordial leads available on Jan. 25, 1945. The R wave in Lead V_2 was unusually small, but a positive decision between a normal variant and an abnormality could not be made in the absence of tracings from precordial Positions 1 and 3. The striking feature of this tracing was the deep cove inversion of the T waves in Leads V_2 and V_4. This pattern brought up the following possibilities: acute anteroseptal ischemia, a small intramural or subepicardial anteroseptal infarct, acute right ventricular dilatation, and pericarditis. Acute right ventricular dilatation was unlikely because the T-wave inversion in transitional Lead V_4 was as great as that in Lead V_2, and pericarditis was unlikely because of the absence of T-wave changes in Lead V_6 and in the standard leads. In the next two tracings, the T waves were tall, upright, and sharply peaked, but the QRS complex showed no significant change other than a slight variation in Leads V_2 and V_4 due to shifting in the transitional zone. The reversal in the T waves of Leads V_2 and V_4 without significant change in the QRS complex was in keeping either with the disappearance of acute anteroseptal ischemia or the healing of a small intramural anteroseptal infarct.[10] In comparison of the QRS pattern on Dec. 30, 1946, with that in previous tracings, it was noted that a significant Q wave had appeared in Lead aV_L, but not in any other lead. An abnormal slurring or notching had developed in the terminal portion of the QRS complex of most leads, affecting the R wave in Leads V_5, V_6, and aV_F and the S wave in Leads V_1 through V_3. This distribution suggested that the slurring or notching was due to a lesion in the last portion of the heart to become activated, namely, the posterobasal wall of the left ventricle. The most striking changes had occurred in the RST-T complex and consisted of abnormal elevation of the junction in Leads aV_F, II, and III and abnormal depression in Leads V_1 through V_4 and in Lead aV_L. The T waves had increased in amplitude in precordial leads over the right ventricle, but became inverted in Leads V_5 and V_6 and showed slight inversion of the terminal phase in Lead aV_F. On the basis of the changes in Leads aV_F and aV_L, a diagnosis was made of recent posterolateral infarction. The depression of the RS-T segment in Leads V_1 through V_3 was considered reciprocal to the elevation in Lead aV_F. On the other hand, the depression of the RS-T segment in Lead aV_L was attributed to extension of the infarct subendocardially into the lateral wall because of the concurrent development of an abnormal Q wave in this lead.

Pathologic Findings.—The heart weighed 443 grams and exhibited a large recent infarct, which involved the entire posterolateral wall of the left ventricle and extended into the septum at the base, as outlined in the roentgenogram reproduced in Fig. 4. By microscopic examination, the infarct was judged to be less than twenty-four hours in age and was found to be transmural in distribution in the lateral as well as in the posterior wall. In view of the pathologic findings,

an abnormal QS or QR complex would have been expected in Lead aV_F. A broadened and notched R wave may have been registered in this lead because of insufficient duration of the degenerative changes in the posterior wall for obliteration of the response to the activating impulse. The

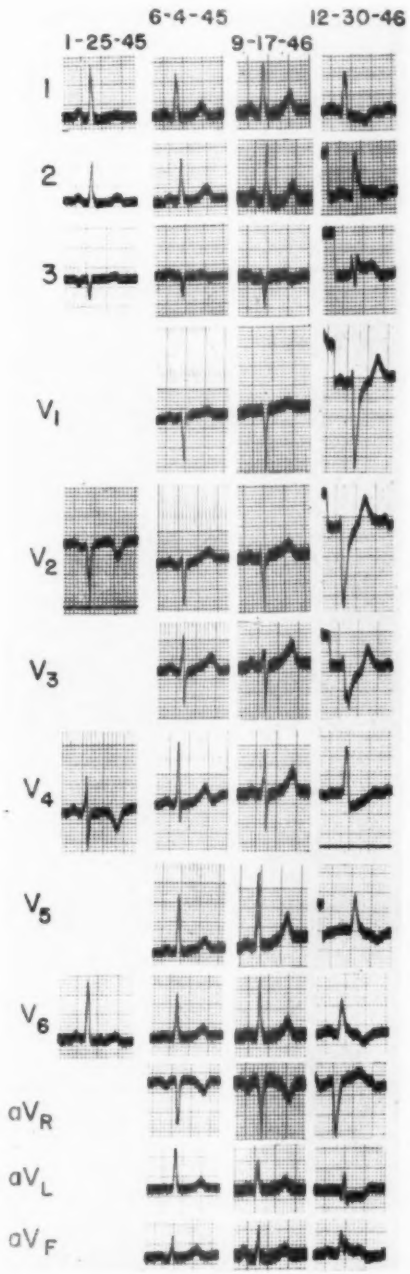


Fig. 3.—Serial electrocardiograms in Case 125, showing recovery from an anteroseptal infarction and a terminal posterolateral infarction.

abnormal QR pattern and depression of the RS-T segment in Lead aV_L might have reflected a more advanced lesion in the subendocardial than in the subepicardial portion of the lateral wall at the time the electrocardiogram was taken. Although the infarct reached the junction of the anterior and lateral walls in the two basilar segments, it is probable that the depression of the RS-T segment in Leads V_1 through V_4 was a reciprocal manifestation of the acute posterolateral infarct. Multiple small areas of fibrosis were found in the subendocardial half of the anteroseptal wall of the left ventricle about midway between apex and base, as indicated by the stippling in Fig. 4, and were considered to be a residue of a healed, patchy, subendocardial infarct. An acute patchy infarct in this area in January, 1945, could have accounted for the T-wave changes in the first tracing, and a subsequent return of a considerable portion of the myocardium to normal could account for the disappearance of all traces of this anteroseptal infarct from the electrocardiogram.

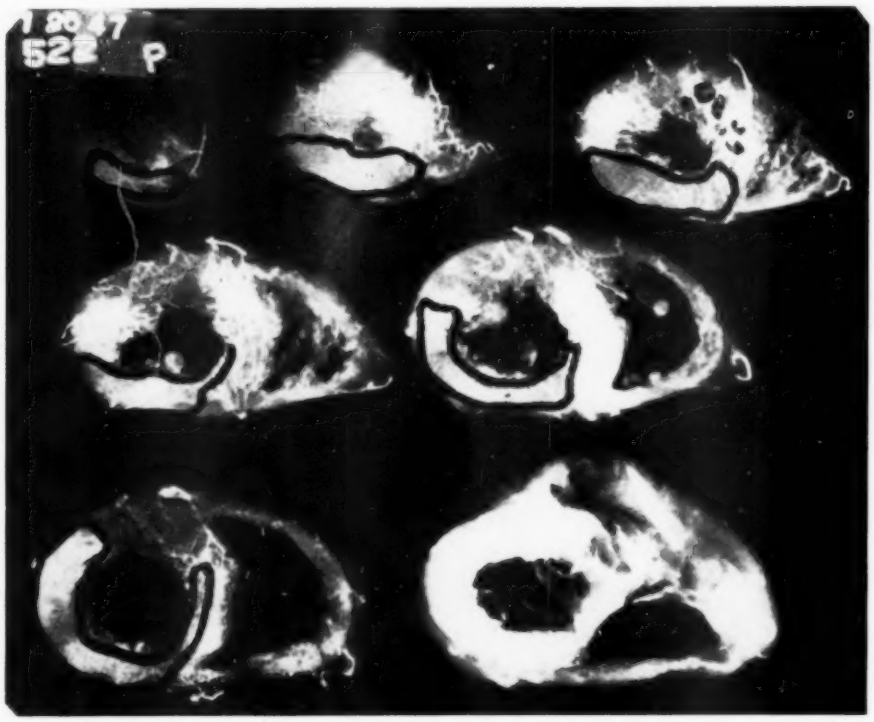


Fig. 4.—Roentgenogram of the injected heart in Case 125 with a large posterolateral infarct demarcated by solid lines and a healed, patchy anteroseptal infarct demarcated by stippling.

CASE 126.—A 55-year-old chronic alcoholic man was in good health until Feb. 16, 1943, when he had an attack of prolonged retrosternal constriction, complicated by congestive failure, and leading to admission two weeks later. The hospital course was uneventful and there were no further cardiovascular symptoms during the remaining year of his life. He returned on Jan. 31, 1944, with a typical history of carcinoma of the stomach, beginning in the fall of 1943. The lesion proved inoperable and resulted in death on April 18, 1944.

Electrocardiographic Findings.—Electrocardiograms reproduced in Fig. 5 were selected from a series obtained during his two hospital admissions. Four cat units of digitalis were given prior to the tracing of March 2, 1943, but the drug was subsequently discontinued. The abnormal QRS-T pattern in Leads II and III of the first electrocardiogram was typical of a recent posterior myocardial infarct. Lead V_6 on this occasion showed a normal R wave, an isoelectric RS-T

junction, and an upright T wave. The subsequent development of a distinct Q wave in Lead V_6, accompanied by reduction in the R wave, transient elevation in the RS-T junction, and inversion of the T wave, indicated extension of the posterior infarct into the lateral wall of the left ventricle. The signs of the lateral infarction did not become evident in the standard leads. The T waves in Leads II and III meanwhile showed deepening inversion typical of an organizing posterior infarct. There was a concurrent reciprocal increase in the height of the upright T waves of Leads V_2 and V_4. On Feb. 1, 1944, there was a shifting supraventricular pacemaker. Comparison of this tracing with those taken the previous year showed no significant change in the abnormal QR complex of Leads II and III. The T waves in Leads II and III were still sharply inverted and comparable in contour to those of the preceding year, but smaller in voltage. Thus, the pattern of organizing posterior infarction had become fixed. Positive findings of posterior infarction were evident in Lead aV_F. On the other hand, the electrocardiographic signs of the lateral extension had disappeared from Lead V_6. The cycle of V_6 from the tracing of February 1,

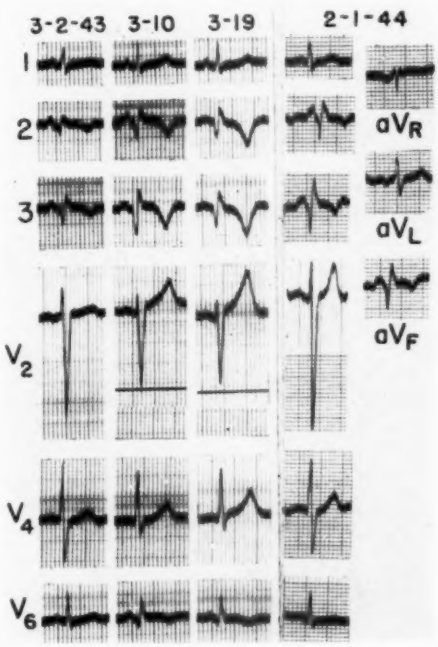


Fig. 5.—Serial electrocardiograms in Case 126.

reproduced in Fig. 5, showed downward drifting of the string between the P wave and the QRS complex, which at first glance might be taken for a Q wave; however, inspection of other cycles in the same lead showed that the Q wave was absent and that the findings in the reproduced cycle represented an artifact from an unstable isoelectric line. The T wave in Lead V_6 had become upright and the entire pattern in this lead, as well as that in Lead I, corresponded closely with that registered in the respective leads of the initial tracing of March 2, 1943.

Pathologic Findings.—The heart weighted 225 grams and revealed an old, competely healed posterolateral infarct, extending from the atrioventricular groove to a point 1.0 cm. above the apex. The infarct was similar in size and distribution to the posterior portion of the infarct which occupied the second, third, fourth, and fifth segments of the heart in Case 125 (Fig. 4). The posterior wall in this area was completely replaced by fibrous tissue and was reduced to a thickness of 2.5 mm., as compared with an average thickness of 13 mm. of the remaining uninfarcted portion

of the left ventricle. Thus, there was good correspondence between the fixed pattern in Lead aV_F and the complete fibrous replacement of the posterior wall. Since this pattern corresponded closely with the reciprocal of that in Lead V_4, it probably represented transmission of cavity potentials through the posterior wall and diaphragm to the left leg. The extension of the infarct into the lateral wall was sufficient to account for the acute changes in Lead V_6 on the first admission. The disappearance of these findings with healing of the infarct was probably due to the fact that the apical portion of the lateral wall was not infarcted and probably exerted the preponderant effects on the potential variations of the electrode at Position V_6.

CASE 127.—A 68-year-old man gave a history of myocardial infarction in 1941, with complete recovery. He had a transient attack of retrosternal oppression on Sept. 8, 1943, and two days

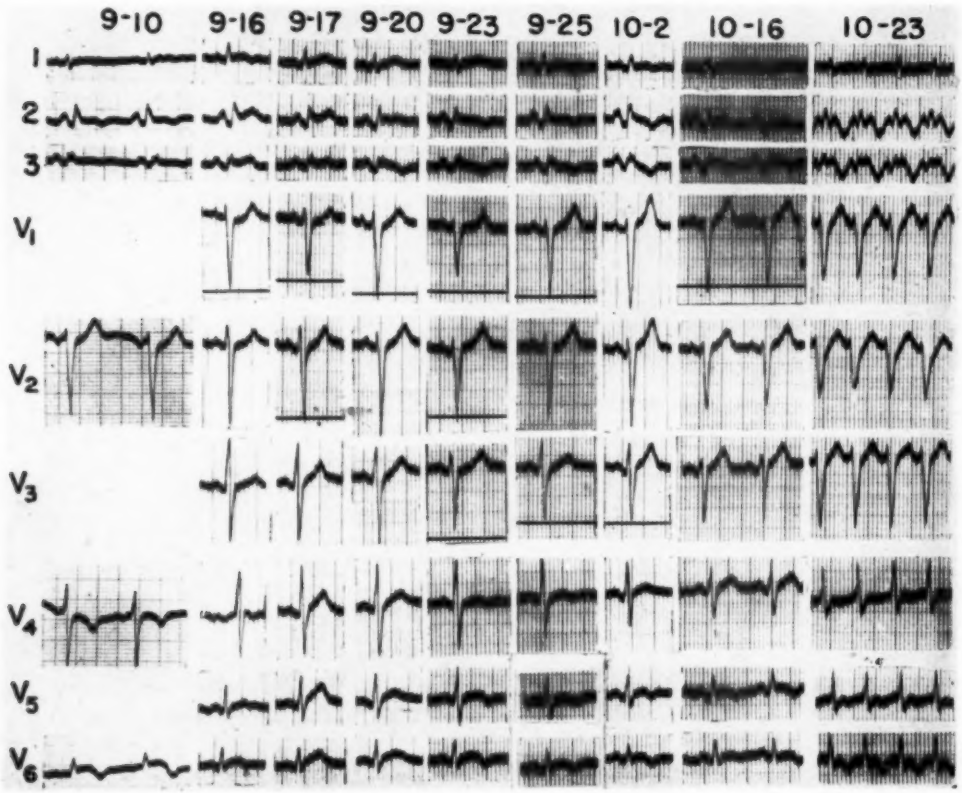


Fig. 6.—Serial electrocardiograms in Case 127.

later was awakened by a more severe episode. After resuming work on September 14, he was seized by a much more severe attack and was brought to the hospital in shock with right hemiparesis. Blood pressure was unobtainable for twenty-four hours. A saddle embolus at the bifurcation of the aorta occurred on September 25, but color gradually returned after Dicumarol therapy. He suddenly collapsed on October 22 with the advent of auricular flutter and died the following day. No cardiac glycosides were given.

Electrocardiographic Findings.—Electrocardiograms reproduced in Fig. 6 include a tracing taken by his family physician on September 10, five hours after the attack of pain which awakened him from sleep. Leads II, III, and V_6 of this tracing showed a small, slurred or notched R wave, an abnormally elevated RS-T junction, and inversion of the terminal portion of the T wave, in-

dicative of a recent patchy infarct of the posterolateral wall of the left ventricle. The inversion of the T wave in Lead V_4 may have been the result of an outlying zone of ischemia, and the apparent depression of the RS-T segment in Lead V_2 was largely an artifact consequent upon an unstable isoelectric line. Although there was no significant change in the QRS complex on September 16, the increased elevation of the RS-T junction and the change to a monophasic upright T wave in Leads II and III suggested further injury to the posterior wall of the left ventricle. Lead aV_F was not obtained until later in the hospital course and at that time showed an abnormal QR pattern of low voltage similar to that of Lead III. The marked elevation of the RS-T junction in Leads V_4 through V_6, which appeared on September 17, might have been due to extension of the lateral portion of the infarct further into the anterior wall or to complicating pericarditis. Because of the absence of significant change in the QRS pattern in these leads in subsequent tracings and the rapid evolution of the T waves in a fashion typical of pericarditis, the RS-T changes in Leads V_4 and V_5 were attributed to extension of the pericarditis into the anterolateral wall. The final tracing on October 23 showed auricular flutter with a 2:1 ratio. There was no evidence to suggest further extension of the posterolateral ventricular infarct.

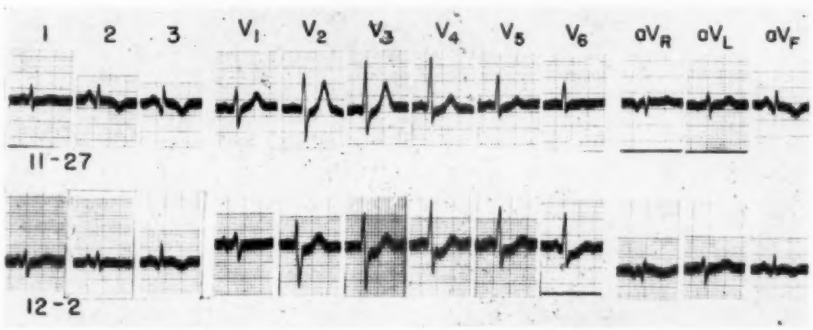


Fig. 7.—Serial electrocardiograms in Case 128.

Pathologic Findings.—The heart weighed 500 grams and exhibited a large, organizing posterolateral infarct, similar in size and position to the lesion in the first five segments in Case 125 (Fig. 4). This infarct was presumably responsible for the abnormalities in Leads aV_F, II, III, and V_6. There was a small, completely healed infarct confined to the anteroseptal aspect of the apical third of the left ventricle. The absence of electrocardiographic signs of this infarct was probably explained by a patchy character and lack of any recent activity. There was a marked fibrinous pericarditis, which was extended onto the anterior aspect of the left ventricle. This was probably responsible for the serial changes in the RS-T segment and T wave beginning on September 17. There was a saddle embolus at the bifurcation of the aorta and a large, residual mural thrombus at the site of the posterolateral infarct.

CASE 128.—A previously healthy 54-year-old man was suddenly seized with retrosternal oppression and dyspnea at 1:00 A. M. on November 26 and was brought to the hospital one hour later. His symptoms were relieved by morphine and his course was uneventful until 7:00 P. M. on December 4, when there was a recurrence of severe retrosternal constriction complicated by shock and followed by death fifteen hours later. No cardiac glycosides were given.

Electrocardiographic Findings.—Electrocardiograms obtained on November 27 and December 2 are reproduced in Fig. 7. An earlier tracing, taken nine hours after the onset of the present illness, showed a wandering pacemaker with episodes of interference dissociation. The QRS pattern in Lead aV_F was similar to that on November 27, which was characterized by a slurred Q wave that was 0.03 second in duration and approximately 50 per cent of the amplitude of the succeeding R wave. This pattern, together with the sharp inversion of the T wave, was typical of an organizing posterior infarct. The R and T waves in the first four precordial leads were unusually tall and the RS-T segments in Leads V_2 through V_4 were abnormally depressed. These

findings constituted classical reciprocal effects of posterolateral infarction. However, Leads V_5 and V_6 in this case showed no definite evidence of involvement of the lateral wall. Lead aV_L apparently reflected the potential variations of the right side of the precordium, rather than the lateral wall of the left ventricle, as judged by its resemblance to Lead V_1. On December 2 an abnormal QR pattern was still present in Lead aV_F. The RS-T junction in this lead remained isoelectric and the T wave was less deeply inverted. A striking change had occurred in the precordial leads and was characterized by the development of marked depression of the RS-T segment in Leads V_6 and V_5 and a significant increase in the downward displacement of the RS-T junction in Leads V_2 through V_4, together with decrease in the voltage of the upright T waves in these leads. Three possibilities were given serious consideration: an acute ischemia of the subendocardial portion of the anterolateral wall, a patchy infarction in this region, and an increased reciprocal effect secondary to further acute injury of the subendocardial portion of the posterolateral wall. The last named seemed less likely because of absence of elevation of the RS-T segment in Lead aV_F. A positive decision could not be reached between the two former possibilities.

Pathologic Findings.—The heart weighed 440 grams and exhibited a recent posterolateral infarct which occupied a position almost identical with that in Case 125 (Fig. 4), except that it was limited to the subendocardial half of the wall. In the second, third, and fourth segments it extended into the subendocardial half of the lateral wall, reaching a point in the lateral wall comparable to that reached in the fifth segment of Fig. 4. The involvement of the subendocardial half of the posterior wall accounted for the abnormal QR pattern in Lead aV_F. The extension into the subendocardial half of the lateral wall may have accounted for the acute depression of the RS-T segment in Leads V_5 and V_6. The findings in Leads V_1 through V_4 were presumably reciprocal, since the infarct did not extend far enough anteriorly to affect directly the pattern in these leads. It is possible, however, that a pathologically unrecognized ischemia of the subendocardial portion of the anterior wall might have accounted for the acute depression of the RS-T segment in the last tracing.

CASE 129.—A 60-year-old man was first admitted to the hospital in August, 1944, because of lobar pneumonia. He had had hypertension and exertional dyspnea for eight years and dependent edema for three years, but gave no definite history of myocardial infarction. He continued to have exertional dyspnea after discharge, but had no chest pain. He remained ambulatory until 7:00 P. M. on March 5, 1945, when he was suddenly seized with severe abdominal pain and vomiting, and was admitted the following morning in collapse. A clinical diagnosis of mesenteric thrombosis was made. Death occurred on March 7.

Electrocardiographic Findings.—Electricardiograms reproduced in Fig. 8 were obtained on Aug. 15, 1944, after the patient's recovery from pneumonia and while he was on maintenance doses of digitalis, and on March 7, 1945, six hours before death, while he was taking no cardiac glycosides. Auricular fibrillation was consistently present. An abnormal QR complex was found in Leads aV_F and aV_L and was indicative of posterolateral infarction. The involvement of the subendocardial portion of the lateral wall was supported by the findings in Leads V_5 and V_6. Although the Q wave in these leads was only 4.0 mm. in depth and about 20 per cent of the amplitude of the succeeding R wave, it was considered abnormal because the time interval from its onset to its nadir was 0.03 second and because of the slurring and prolongation of the ascending limb of the R wave. Esophageal leads were obtained in order to investigate further the lesion of the posterior wall. Leads at the ventricular level showed an initial Q wave, 3.0 to 5.0 mm. in depth, 0.03 to 0.04 second in duration, and 25 to 50 per cent of the amplitude of the succeeding R wave. These findings, together with the slurring of the ascending limb of the R wave, were regarded as confirmatory evidence of infarction of the subendocardial portion of the posterior wall. The abnormal Q waves in Leads I and II were due as much to the initial positivity of the right arm as to the initial negativity of the left arm and leg. Although a QR complex indicative of posterior infarction was recorded in Lead aV_F, an RS deflection, in no way suggestive of posterior infarction, was registered in Lead III. Since the RS complex in Lead III was the approximate reciprocal of the QR pattern in Lead aV_L, it would appear that the potential variations of the left arm component of Lead III preponderated over those of the left leg component in this case. From the contour of the T waves, it was believed that the posterolateral infarct was old and

healed. The R wave did not show the expected increase in amplitude as the electrode was moved from precordial Positions 1 to 3 and actually was very slightly smaller in Lead V_2 than in Lead V_1. Although this finding was in keeping with an old, completely healed anteroseptal infarction, it was not sufficiently striking to justify the diagnosis. The inverted T waves in Leads V_2 and V_3 on August 15, 1944, were not typical of infarction, but were not satisfactorily accounted for. In the tracing of March 7, 1945, there was no significant change in the QRS pattern in the limb leads or in Leads V_5 and V_6. Signs of the old, healed posterolateral infarction were still evident in Leads aV_F, aV_L, V_5 and V_6. The only significant change occurred in the first four precordial leads. The initial phase of the QRS complex was upright in the first three precordial leads and averaged 4.0 mm. in Leads V_1 and V_2 but fell off to 2.0 mm. in Lead V_3. In Lead V_4 there was a 1.0 mm. Q wave followed by an R wave, which averaged 7.0 millimeters. The RS-T junction was elevated approximately 1.0 mm. in Leads V_1 through V_3 and was isoelectric in Lead V_4. The T wave was sharply inverted in these leads and reached its greatest depth in Lead V_3. The question arose as to whether these changes were representative of a recent anteroseptal infarct, an old anteroseptal infarct with recent reinfarction or ischemia, or acute right ventricular dilata-

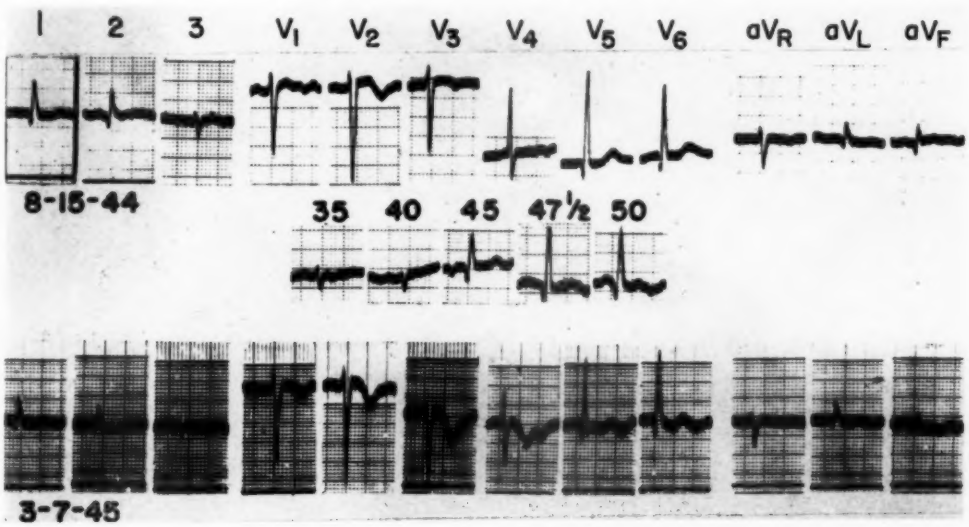


Fig. 8.—Serial electrocardiograms in Case 129, showing old, healed posterolateral infarction and terminal anteroseptal infarction. The tracings in the middle row are esophageal leads at indicated levels.

tion. The last named was considered less likely because the maximal T-wave inversion was found in Leads V_3 and V_4 rather than in V_1 and V_2 and, more important, because it failed to account for the abnormalities in the initial phase of the QRS complex in Leads V_3 and V_4. These changes pointed toward a recent, patchy subendocardial infarct in the anteroseptal portion of the left ventricle.

Pathologic Findings.—Death was due to thrombosis of the superior mesenteric artery. The heart weighed 676 grams and revealed multiple old infarcts, situated as outlined in Fig. 9. In the apical segment there was a semilunar infarct involving the subendocardial half of the anterolateral and posterior walls. Higher in the ventricle the infarct was divisible into three separate portions. The largest occupied the subendocardial one-half to two-thirds of the posterior wall and extended from apex to base. A second infarct involved the subendocardial one-half to two-thirds of the lateral wall in the fourth and fifth segments and became more anterior at the base. Microscopic examination of these two infarcts at various levels showed patchy to dense fibrosis without evidence of recent activity. A third infarct was located in the subendocardial one-third

to one-half of the anteroseptal area, as demarcated by broken lines in Fig. 9. Microscopic examination of this lesion showed patchy fibrosis, which was a residue of a remote infarction with recent cellular infiltration, which was attributed to terminal reinfarction. Thus, the pattern in Lead aV_F and the esophageal leads could be correlated with the old, subendocardial posterior infarction, whereas that in Leads aV_L, V_5, and V_6 corresponded with the old, subendocardial lateral infarction. The acute changes in the first four precordial leads on March 7, 1945, were apparently the result of acute infarction in an area of old, healed anteroseptal fibrosis. This was regarded as secondary to the vascular collapse produced by the mesenteric thrombosis.

CASE 130.—A 45-year-old woman was perfectly well until 11:00 P. M. on Oct. 31, 1944, when she was suddenly taken with sharp retrosternal pain, lasting about one-half hour, accompanied by cough and followed by gross hemoptysis. There was no clinical evidence of phlebothrombosis or pulmonary embolism. Physical examination revealed hyperthyroidism, later confirmed by

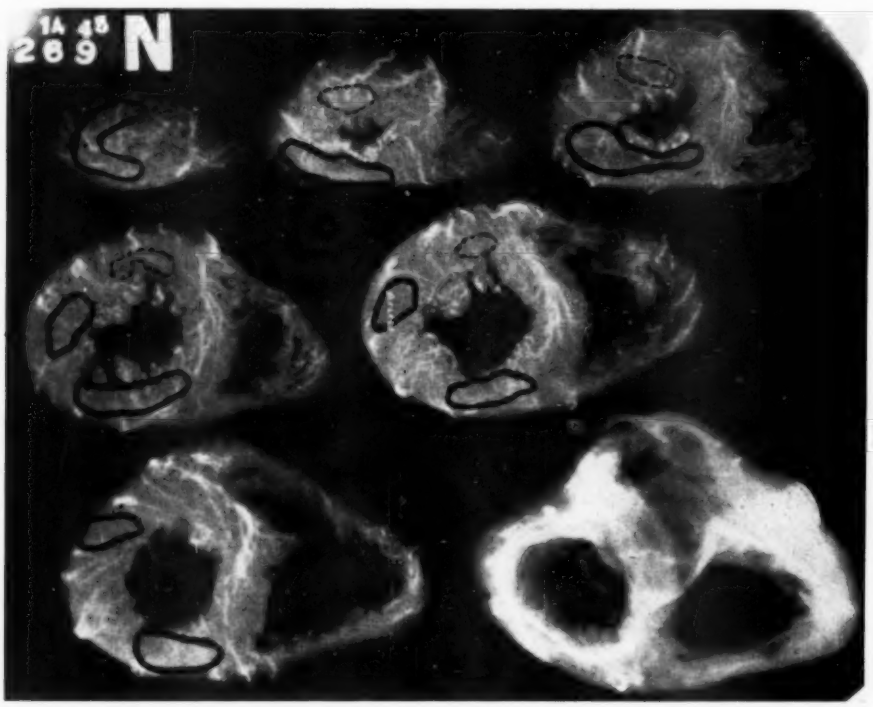


Fig. 9.—Roentgenogram of the injected heart in Case 129, showing old, healed posterolateral infarction in solid outline and recent patchy anteroseptal infarction in broken outline.

the basal metabolic rate. After a month in the hospital, the patient failed to report for observation for a year, when she returned in thyroid crisis and died on Nov. 25, 1945. No cardiac glycosides were given.

Electrocardiographic Findings.—An electrocardiogram reproduced in Fig. 10, *A* was taken thirty-six hours after the onset of the attack of retrosternal pain. The Q wave recorded in Lead aV_F was 0.02 second in duration, 2.5 mm. in depth, and one-third of the amplitude of the succeeding R wave. From this borderline Q wave, together with the associated elevation of the RS-T segment, a diagnosis of recent posterior infarction was made. A borderline QR complex with a ratio of 20 per cent was found in Leads V_5 and V_6. Because of the abnormal elevation of the RS-T segment in these leads, the findings were attributed to extension of the infarct subendocardially into the lateral wall of the left ventricle. Lead aV_L showed an RS pattern like that of Lead V_4 and thus gave no help in the delineation of the lateral infarction. However, the diag-

nosis of posterolateral infarction was confirmed by the classical evolution of the RST-T pattern in Leads aV_F, V_5, and V_6 of serial tracings over the next month. Leads II and III also revealed signs of posterior infarction. The distinct Q wave in Lead I was not due to initial negativity of the left arm, since no Q wave was demonstrable in Lead aV_L. It was a manifestation of initial positivity of the right arm, as shown by its correspondence with the reciprocal of the pattern in Lead aV_R.

Pathologic Findings.—The heart weighed 449 grams and revealed an old, healed posterolateral infarct with an overlying organized pericarditis. The distribution of the lesion in the first, second, fourth, and fifth segments was almost identical with that in the corresponding segments in Case

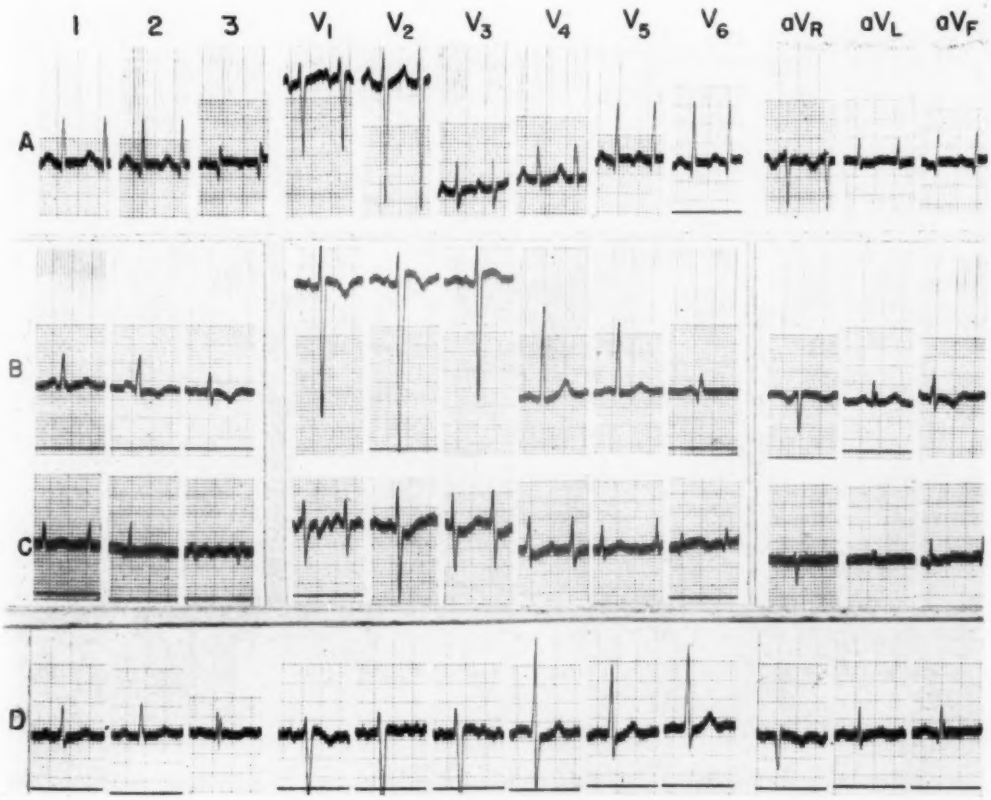


Fig. 10.—Electrocardiographic findings in posterolateral infarction. *A*, **Case 130;** *B*, **Case 131;** *C*, **Case 132; and** *D*, **Case 133.**

132 (Fig. 11). In the third segment in this case, the infarct did not extend as far into the lateral wall as in this segment in Case 132. Thus, there was good correlation between the electrocardiographic findings and those at necropsy.

CASE 131.—A 59-year-old woman gave a history of a sudden onset of severe retrosternal constriction and dyspnea four months previously, leading to hospitalization elsewhere. With resumption of ambulation, angina pectoris occurred. During the fortnight immediately preceding entry, she had repeated paroxysms of nocturnal dyspnea. There was marked pulmonary congestion and edema on admission, but no evidence of right heart failure. Compensation was gradually restored, but congestive failure recurred after discharge, ending in death three months later.

Electrocardiographic Findings.—An electrocardiogram reproduced in Fig. 10, *B* was obtained on the fifth hospital day, after the administration of a total of 1.4 Gm. of digitalis. In Lead aV_F there was an initial Q wave 1.0 mm. deep and approximately 15 per cent of the succeeding R wave. Although the QR ratio was within normal limits, the association of a definite Q wave with notching and prolongation of the ascending limb of the R wave indicated that the QR complex was abnormal. These findings were interpreted as evidence of patchy infarction of the posterior wall of the left ventricle. The isoelectric RS-T junction and inverted T wave in Lead aV_F were most likely a residue of an old infarct, but were compatible with the stage of organization. The findings in Lead aV_F carried over into Leads II and III. In Lead aV_L there was a Q wave of 0.5 mm., fol-

Fig. 11.—Roentgenogram of the injected heart in Case 132, showing the position of the posterolateral infarct.

lowed by a precipitous upstroke and then a coarse, broad notch on the downstroke of the R wave. The QRS pattern in this lead was thus abnormal, but was not specific for infarction. On the other hand, the presence of a Q wave in Lead V_6 after an upright initial deflection in the other five precordial leads, together with a marked reduction in the amplitude of the R wave in Lead V_6 in comparison with that of Lead V_5, was indicative of extension of the posterior infarct into the lateral wall of the left ventricle. The Q wave in Lead V_6 was 2.0 mm. deep and approximately 50 per cent of the succeeding R wave. The RS ratio in the first three precordial leads indicated that the electrode was to the right of the interventricular septum. The R wave of Lead V_2 was slightly smaller than that of Leads V_1 and V_3, but the reduction was not sufficiently great

to be of diagnostic significance. Although inversion of the T wave in Leads V_1 and V_2 may occur as a normal variant, the elevation of the RS-T junction in these leads suggested that the RS-T segment and T complexes were abnormal. The T-wave changes in Leads V_1 and V_2 were considered independent of digitalis because of the contour of the RS-T segment and because the Q-T interval was at the upper limit of normal. The diagnosis rested between acute anteroseptal ischemia, a recent intramural anteroseptal infarction, and acute right ventricular dilatation. The last alternative was favored because of the maximal T-wave changes in Lead V_1 and was compatible with the marked pulmonary congestion and edema still present at the time the electrocardiogram was taken.

Pathologic Findings.—Necropsy revealed considerable left ventricular hypertrophy and disclosed an old, completely healed infarct of the posterolateral aspect of the apical portion of the left ventricle, comparable in size and position with that in Case 132 (Fig. 11). From its position, the infarct adequately accounted for the abnormal patterns in Leads aV_F and V_6. Since the anterior walls of the left ventricle and septum were not infarcted, the findings in Leads V_1 and V_2 were due either to acute right ventricular dilatation or anteroseptal ischemia, more likely the former.

CASE 132.—A 64-year-old woman was admitted to the hospital because of gangrene of the left leg. She gave a typical history of angina pectoris of two years' duration. No definite history of myocardial infarction or of cardiac failure could be elicited. The patient died of a cerebral vascular accident on the twentieth hospital day.

Electrocardiographic Findings.—An electrocardiogram obtained on the third hospital day, after the administration of 1.1 Gm. of digitalis, is reproduced in Fig. 10, *C*. Auricular fibrillation was present with a rapid ventricular rate. The initial phase of the QRS complex was upright in the first five precordial leads and the R wave was relatively tall in Leads V_1 through V_3. The marked reduction in the R wave and the appearance of a relatively large Q wave as the electrode was moved from Position 5 to Position 6 was indicative of infarction of the lateral wall of the left ventricle. The elevation of the RS-T junction and the monophasic upright T wave suggested a recent lesion. The depression of the RS-T segment in Leads V_2 through V_4 might have been reciprocal to the elevation in Lead V_6 or could have been a manifestation of digitalis action. No evidence of the lateral infarction was registered in Lead aV_L or in the standard leads. The small, notched QRS complex in Lead aV_L suggested that the potential variations of the anterior aspect of the left ventricle near the transitional zone were being referred to the left arm. In Lead aV_F, however, there was a QR complex, the Q wave ranging from one-fourth to one-third of the amplitude of the R wave. This was a borderline finding, which was suggestive, but not diagnostic, of extension of the lateral infarct into the posterior wall of the left ventricle. Thus, the electrocardiogram was diagnostic of lateral infarction and suggestive of coexistent posterior infarction.

Pathologic Findings.—The heart weighed 362 grams and revealed an old, completely healed infarct of the apical three-fifths of the posterolateral aspect of the left ventricle, as outlined in Fig. 11. The infarct was limited to the subendocardial one-half to three-fourths of the posterior wall, but was transmural in a portion of the lateral wall. There was good correspondence between the abnormal QR pattern in Lead V_6 and the lesion of the lateral wall. There was an overlying chronic epicarditis, which might have been a factor in the elevation of the RS-T segment and the monophasic upright T wave. It is also possible that this was a fixed pattern associated with an old, completely healed lateral infarct. The borderline QR complex in Lead aV_F was apparently a manifestation of the posterior portion of the infarct.

CASE 133.—A 38-year-old man was hospitalized because of mental confusion and convulsions due to hypertensive encephalopathy. He had had hypertension for ten years and had been treated in another hospital five years previously for coronary thrombosis. There was no history of subsequent infarction or angina pectoris. Maintenance doses of digitalis had been instituted before admission and were continued during hospitalization. Death from bronchopneumonia occurred on the twenty-eighth day.

Electrocardiographic Findings.—An electrocardiogram obtained upon the first hospital day is reproduced in Fig. 10, *D*. The prominent R wave in Leads V_4 through V_6, together with the 0.05 second interval from onset to peak of this deflection, suggested left ventricular hypertrophy. The T-wave pattern, however, was not characteristic. The Q wave recorded in Lead aV_F was 0.02 second in duration, 1.5 mm. in depth, and 25 per cent of the succeeding R wave. The ascending limb of the R wave was fairly steep, consuming 0.03 second from onset to peak, but the descending limb was coarsely notched. The QR pattern in Lead aV_F was borderline and was somewhat suggestive of a subendocardial posterior infarction. In Lead aV_L there was coarse notching of the ascending limb of the R wave. This, together with a time interval of 0.07 second from onset of the QRS complex to the peak of the R wave, was distinctly abnormal and compatible with, though not diagnostic of, a conduction defect in the lateral wall of the left ventricle. These findings, taken in conjunction with those in Lead aV_F, were suggestive of an old, subendocardial posterior infarction, extending in patchy fashion through the lateral wall of the left ventricle.

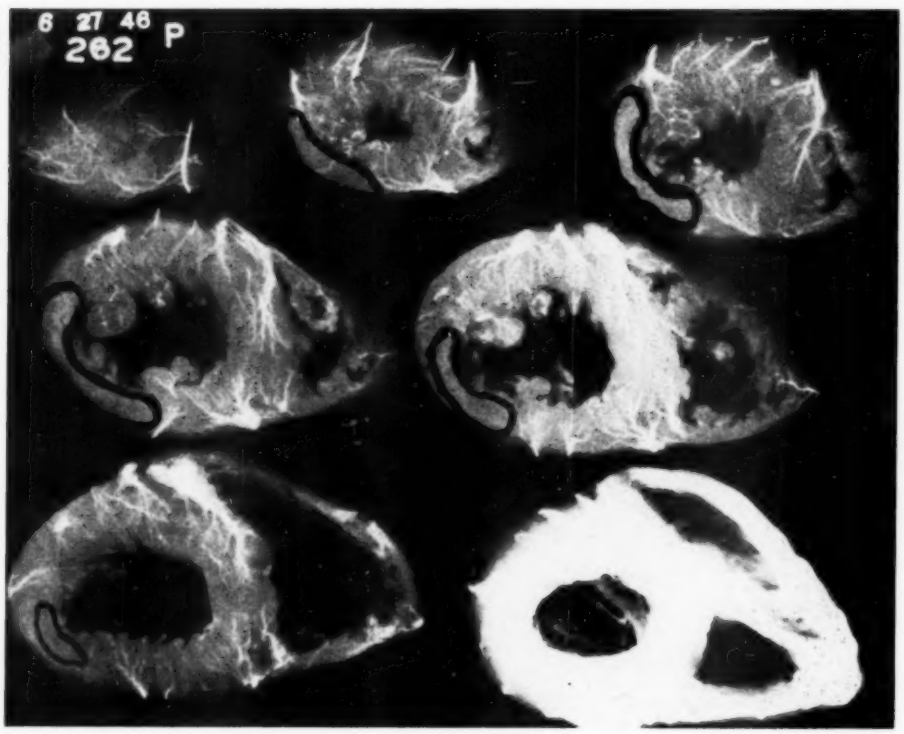


Fig. 12.—Roentgenogram of the injected heart in Case 133, showing the position of the posterolateral infarct.

Pathologic Findings.—The heart weighted 788 grams and exhibited an old, completely healed posterolateral infarct, as outlined in Fig. 12. Portions of the infarct were transmural and other portions were limited to the subendocardial two-thirds. Microscopic examination revealed islands of intact muscle interspersed through the infarct. This, together with the lack of high axillary leads, may have accounted for the paucity of electrocardiographic findings. Defective conduction through the lateral and posterior walls of the left ventricle secondary to the infarct could explain the pattern in Leads aV_L and aV_F. A fibrinous pericarditis secondary to uremia was found at autopsy. This may have accounted for the presence of upright, rather than the usual inverted, T waves in Leads V_4 through V_6 associated with the QRS pattern of left ventricular hypertrophy.

CASE 134.—A 56-year-old man, who had had hypertension for at least four years, was suddenly seized with extreme dyspnea while driving his car. Chest pain was denied. He was brought directly to the hospital and arrived moribund in left ventricular failure. Death occurred on the third hospital day.

Electrocardiographic Findings.—The electrocardiogram is not reproduced because of its close resemblance to that in Case 133 (Fig. 10, *D*). The QRS pattern in the precordial leads was typical of left ventricular hypertrophy. Abnormal depression of the RS-T segment was found in the precordial leads over the left ventricle and was attributed in part to left ventricular hypertrophy and in part to superimposed effects of 0.8 mg. of Cedilanid, administered before the electrocardiogram was obtained. In Lead aV_L there was coarse slurring at the base of the ascending limb of the R wave in place of the notching in the corresponding lead of Fig. 10, *D*. The delayed attainment of the peak of the R wave, depressed RS-T junction, and inverted T wave of this lead were ascribed to left ventricular hypertrophy. In Lead aV_F, there was an initial Q wave followed by a coarsely notched M-shaped R wave. The Q/R ratio was 33 per cent. These changes were attributed to defective conduction in the posterior wall, secondary to subendocardial infarction. Because of the type of QRS pattern and the lack of typical changes in the RS-T segment and T wave, it was postulated that the infarct was old and healed.

Pathologic Findings.—The heart weighted 1,104 grams as a result of extreme left ventricular hypertrophy. Old healed infarcts were found in the posterior and lateral aspects of the left ventricle, which corresponded closely in distribution to the lesions in Case 129 (Fig. 9), demarcated by solid lines. At the apex there was a single infarct occupying the subendocardial half of the posterolateral wall. Toward the base, this infarct split into two separate lesions, a patchy posterior infarct, similar in position to that of Fig. 9, and a somewhat denser infarct of the subendocardial half of the lateral wall. This infarct, like that in Case 129, shifted into a more anterolateral position at the base. The type of lesion in the posterior wall found at autopsy corresponded closely with the electrocardiographic findings in Lead aV_F. The lateral infarct had been missed electrocardiographically, probably because it occupied a relatively small portion of the markedly hypertrophied lateral wall.

CASE 135.—A 42-year-old man had had transient attacks of retrosternal oppression, provoked by exercise and relieved promptly by rest, for fifteen years and was admitted to the hospital following three weeks of almost continuous angina decubitus. There were physical signs of rheumatic aortic stenosis and insufficiency complicated by hypertension. The patient continued to have prolonged attacks of chest pain during his hospital stay and died on the tenth day.

Electrocardiographic Findings.—An electrocardiogram obtained four hours after admission and before the administration of digitalis was reproduced in a previous communication.[7, Fig. 7, Case 16] In Lead V_6 there was a prominent slurred R wave, a slightly delayed intrinsicoid deflection, a depressed RS-T junction, and an inverted T wave, which were considered typical of left ventricular hypertrophy. The diagnosis was supported by the exceptionally deep, slurred S wave in Leads V_1 through V_3. Lead aV_L displayed a minute Q wave 0.5 mm. in depth and 0.02 second in duration, followed by a slurred ascending limb of the R wave, 11 mm. in height and 0.06 second in duration. The RS-T junction was isoelectric and the T wave was inverted. The QRS pattern in Lead aV_L was indicative of defective conduction in the lateral wall of the left ventricle and might have been the result of left ventricular hypertrophy with patchy fibrosis or a patchy infarction of the lateral wall of the left ventricle. Lead aV_F exhibited a QS complex with marked slurring and notching of its terminal limb. The question arose as to whether the findings in Lead aV_F were the result of a posterior infarct or were merely due to horizontal position with transmission of potential variations of the posterior inferior surface of the right ventricle to the left leg. The former alternative was preferred in the ante-mortem interpretation because of the late R equivalent and a diagnosis was made of posterolateral infarction, probably old.

Pathologic Findings.—The heart weighed 602 grams as a result of left ventricular hypertrophy secondary to rheumatic aortic stenosis and exhibited an organizing posterolateral infarct of one to two months' duration. The infarct involved the second and third segments in a fashion comparable to that in the corresponding segments in Case 133 (Fig. 12). The involvement of the

fourth segment was closely comparable, both in size and position, to the lesion in the fifth segment of Fig. 12. On microscopic examination, the infarct appeared dense in the subendocardial one-fourth and patchy in the remainder of the wall. The findings in Lead aV_L could be correlated satisfactorily with the lateral portion of the infarct. On restudy of the case, however, it is doubtful that the posterior part of the infarct was responsible for the findings in Lead aV_F, since too small a fraction of the posterior wall was involved to account for a QS complex. It is more likely that the heart was in horizontal position and that the QS complex recorded in Lead aV_F was transmitted from the epicardial surface of the posteroinferior aspect of the right ventricle to the left leg.

CASE 136.—A 52-year-old man was first admitted to the hospital three days after the onset of a prolonged attack of oppressive retrosternal pain. Convalescence was uneventful and the patient had no further attacks of thoracic pain. Seventeen months later he was readmitted with typical signs of a saddle embolus at the bifurcation of the aorta complicated by acute left ventricular failure. Death occurred nine hours after the onset of symptoms referable to the saddle embolus.

Electrocardiographic Findings.—Electrocardiograms taken during the first admission included only the three standard limb leads and precordial Leads V_2, V_4, and V_6. Five tracings taken over a period of two weeks showed a constant QRS-T pattern in the standard leads. This consisted of a prominent R_1 and an upright T_1; a triphasic QRS complex in Lead II, consisting of a 1.0 mm. Q wave, a 6.0 mm. R wave, and a 1.0 mm. S wave, with an isolectric RS-T segment and an upright T wave; and a notched QS complex with a slightly elevated RS-T segment and a low upright T wave in Lead III. Although the QRS pattern in Leads II and III was suggestive of posterior infarct, the absence of serial changes in T_2 and T_3 left the diagnosis in doubt. However, the precordial leads taken during the first week showed a marked depression of the RS-T segment, maximal in Lead V_2 and comparable to that present in corresponding leads of the tracing of December 2 of Fig. 7 (Case 128). During the second week of hospitalization, the RS-T junction approached the isoelectric line and the R and T waves increased considerably in amplitude, especially in Lead V_2; this finding was comparable to that in the precordial leads of November 27 of Fig. 7. The changes in the precordial leads were typical of the reciprocal effects produced by recent posterolateral infarction. The electrocardiogram taken on his final admission revealed auricular fibrillation with numerous ventricular premature beats from multiple foci. The duration of the QRS complex in the beats of superventricular origin was 0.12 second. The initial deflection of the supraventricular beats was upright in all precordial leads and in aV_L and aV_F. The R wave was coarsely slurred and prolonged in precordial leads over the left ventricle. This was interpreted as evidence of incomplete left bundle branch block. Lead aV_F displayed a small initial R wave followed by a broad, notched S wave. This was attributed to transmission of the potential variations of the epicardial surface of the posteroinferior aspect of the right ventricle to the left leg, as a result of horizontal position of the heart. Thus, Lead aV_F and the standard leads showed no evidence of the posterolateral infarct which had occurred seventeen months previously.

Pathologic Findings.—The heart weighed 655 grams and revealed a healed infarct occupying the posterolateral aspect of the basal two-thirds of the left ventricle. This infarct was comparable in position and size to that in the third, fourth, fifth, and sixth segments in Case 125 (Fig. 4). Microscopic examination revealed that the involvement was dense in the subendocardial one-third and patchy in the remainder of the wall. The posterior portion of the infarct was probably missed in Lead aV_F because of the horizontal position of the heart with transmission of potential variations of the posteroinferior surface of the right ventricle to the left leg. The infarction of the lateral wall was probably missed because of the incomplete left bundle branch block.

CASE 137.—An 87-year-old man was admitted to the hospital because of senile dementia complicated by bronchopneumonia. No past history was obtainable. Death occurred on the fourth hospital day from pneumonia.

Electrocardiographic Findings.—An electrocardiogram on the second hospital day showed auricular fibrillation. The QRS interval was within normal limits. Leads V_5, V_6, and aV_L

displayed a tall, slurred, initial R wave, depressed RS-T junction, and shallow inversion of the T wave, interpreted as evidence of left ventricular hypertrophy. In Lead aV_F there was a slurred QS complex, 3.0 mm. in depth, followed by a low upright T wave. The question arose as to whether this was a remnant of an old posterior infarct or whether it was merely the result of transverse position and due to transmission of potential variations of the right ventricle to the left leg. The former alternative was preferred in the ante-mortem interpretation, but the patient's condition did not permit further investigation by means of esophageal leads and by repetition of Lead aV_F in different postures.

Pathologic Findings.—The heart weighed 508 grams and revealed an old, completely healed infarct confined to the posterolateral aspect of the left ventricle in the apical two segments. The lesion was comparable in position to that in the corresponding segments in Case 132 (Fig. 11), but was slightly smaller in size and was confined to the subendocardial one-half of the wall. The lateral portion of the infarct was not detectable in Leads V_5, V_6, and aV_L, probably because of the relatively small size of the lesion in comparison with the mass of uninfarcted hypertrophied lateral wall of the left ventricle. The QS complex in Lead aV_F, which had led to the ante-mortem diagnosis of posterior infarct, was probably not a manifestation of the posterior infarct found at autopsy because of the relatively small size and subendocardial location of the latter. It is more likely that this QS complex was due to transmission of the potential variations of the right ventricle to the left leg.

COMMENT

Interpretation of Lead aV_L.—When a QR or QS complex is recorded in Lead aV_L, determination of the cardiac position is an important prerequisite to the interpretation of the findings. This is accomplished through a study of the QRS pattern in the unipolar limb leads in reference to that in the precordial or other semidirect leads, as discussed in detail in a previous communication.[11] On the basis of the findings in Lead aV_F, the position of the heart in a given case can usually be classified into one of the following two groups: (a) horizontal to semihorizontal, and (b) vertical to intermediate. The cardiac position falls within the former range when Lead aV_F displays either (1) a small R and deep S wave, (2) an equiphasic RS complex, (3) an RSR′ pattern, or (4) a QS pattern not due to extensive posterior infarction.[8] The cardiac position falls within the latter range when Lead aV_F exhibits (1) a prominent R wave with a relatively small Q and/or S wave, (2) a monophasic upright deflection, and (3) an abnormal QR or QS pattern attributable to posterior infarction.[8]

(a) *Differentiation of the Normal and Abnormal QR Complexes in Lead aV_L in Horizontal to Semihorizontal Position of the Heart*: Under these circumstances, the potential variations of the left arm are transmitted principally from the epicardial surface of the free wall of the left ventricle. In the vast majority of the cases, especially when the apex is directed anteriorly, the lateral wall of the left ventricle faces toward the left arm and constitutes the main source of the QRS-T pattern recorded in Lead aV_L. In some cases, particularly when the apex is displaced backward, the basal aspect of the posterior or posterolateral wall may face toward the left arm and thus may exert the predominant effect upon the potential variations of the left arm.

The decision as to whether the potential variations of the left arm were transmitted chiefly from the lateral or from the posterobasal wall of the left ventricle was of some importance in the evaluation of borderline QR patterns

in Lead aV_L, because of the fact that the normal Q wave, registered through esophageal leads opposite the posterobasal wall of the left ventricle, is slightly longer in duration and slightly larger in proportion to the succeeding R wave than the normal Q wave registered through axillary leads opposite the lateral wall, because of the later onset of activation of the posterobasal wall. Thus, the normal Q wave in Leads V_5, V_6, and also in aV_L (if the potential variations of the left arm are transmitted chiefly from the lateral wall of the left ventricle) measures 0.02 second or less from onset to nadir, and is less than 25 per cent of the amplitude of the succeeding R wave. On the other hand, the normal Q wave in esophageal leads opposite the posterobasal wall of the left ventricle and also in aV_L (if the potential variations of the left arm are derived mainly from this portion of the heart) may reach 0.03 second in duration and may approach 25 per cent of the amplitude of the succeeding R wave.

Indirect evidence of the chief source of the QRS pattern in Lead aV_L may be obtained from (1) the direction of the associated P wave, provided sinus rhythm is present, and (2) the contour of the QRS complex in Lead aV_R. When the epicardial surface of the lateral wall of the left ventricle faces toward the left arm, the potential variations of the lower part of the lateral aspect of the left atrium are transmitted through the lateral wall of the left ventricle to the axilla and left arm, resulting in an upright P wave with gradually sloping limbs in Lead aV_L, resembling that in Leads V_5 and V_6. Backward rotation of the heart favors transmission of the potential variations of more of the posterior wall of the left atrium to the left arm, resulting in a diphasic to inverted P wave with a steep downstroke, reminiscent of the diphasic to inverted P waves with prominent intrinsicoid downstroke registered through esophageal leads behind and above the left atrium.

When the heart is rotated on its transverse axis, so as to carry the apex backward and tilt the base upward, transmission of the potential variations of the posterobasal aspect of the left ventricle is prone to occur toward the right as well as the left arm, resulting in a prominent late R wave in Lead aV_L. Such a finding in Lead aV_R suggests, but does not necessarily imply, that an associated QR complex in Lead aV_L is derived from the potential variations of the posterobasal aspect of the left ventricle. On the other hand, the absence of this late R wave from Lead aV_R or the presence of a rudimentary late upstroke in this lead constitutes negative evidence suggesting that the QR complex in Lead aV_L was not derived from the posterobasal, but rather from the lateral, wall of the left ventricle.

A QR complex of 0.5 millivolt or more in Lead aV_L, transmitted from the epicardial surface of either the lateral, posterolateral, or posterobasal aspect of the left ventricle, may be considered abnormal and referable to infarction when (1) the time interval from onset to nadir of the Q wave is more than 0.03 second and the Q/R ratio exceeds 25 per cent, and (2) the Q wave is followed by an upstroke that is notched or coarsely slurred and consumes 0.05 second or more from onset to nadir. If the voltage of the QRS complex is below 0.5 millivolt, the Q/R ratio and the contour of the ascending limb of the R wave become less significant and the tracing is classed as borderline unless the time interval from

onset to nadir of the Q reaches 0.04 second or that from onset to peak of R reaches 0.06 second. The significance of QR complexes of 0.5 millivolt or more with a Q-wave duration of 0.02 to 0.03 second depends upon the portion of the heart chiefly responsible for the pattern in Lead aV_L. If Lead aV_L reflects the potential variations of the lateral wall of the left ventricle, these findings may be considered abnormal when accompanied by a Q/R ratio over 25 per cent; otherwise they may be considered borderline. If Lead aV_L reflects the potential variations of the posterobasal wall of the left ventricle, these findings may be considered borderline in the presence of a Q/R ratio above 25 per cent, and otherwise normal. A deep QS complex is a very rare finding in Lead aV_L of a semihorizontal to horizontal heart and would point to complete transmural infarction, provided one could be certain that the potential variations of the left arm were transmitted from the epicardial surface of the left ventricle and not from the mitral orifice, in the manner to be discussed.

(b) *Differentiation of the Normal and Abnormal QR Complexes in Lead aV_L in Vertical, Semivertical, or Intermediate Position of the Heart*: When the heart is in intermediate position, the epicardial surface of the lateral wall of the left ventricle generally faces toward the left arm. The derivation of the potential variations of the left arm is comparable to that when the heart is in horizontal to semihorizontal position and rotated so that the lateral aspect of the left ventricle is directed toward the left arm. The findings in Lead aV_L, both in the presence and absence of lateral infarction, and the criteria for the differentiation of the abnormal and normal QR complexes are consequently similar to those previously described.

Vertical to semivertical position of the heart is generally accompanied by sufficient clockwise rotation about the longitudinal axis so that the potential variations of the anterior wall of the right ventricle or anterior terminus of the septum are transmitted to the left arm. Under these circumstances, infarction of the lateral wall of the left ventricle is not detectable in Lead aV_L. The usual findings in this lead consist of either a small R and deep S wave, an equiphasic RS, or a multiphasic RSR′ complex, resembling patterns in precordial leads over the right ventricle or at the transitional zone.

When vertical to semivertical position is accompanied by counterclockwise rotation, rather than the usual clockwise rotation about the longitudinal axis, the potential variations of the left ventricular cavity may be transmitted through the mitral orifice and left atrium to the left arm. As a consequence, Lead aV_L displays a deep and prolonged Q wave, representing negative potentials from the left ventricular cavity, usually followed by a late R wave, derived from activation of the posterobasal wall of the left ventricle.[11] The Q wave is large and the R wave small or absent, as in esophageal leads above the heart, when the predominant pathway to the left arm is through the roof of the left atrium, and the Q wave is less prolonged and less deep and the R wave taller, as in esophageal leads behind the left atrium, when the predominant pathway to the left arm is through the posterior wall of the left atrium. The QR or QS complex, which occurs as a normal variant in Lead aV_L in a semivertical to vertical heart, rotated counterclockwise on its longitudinal axis, may be identical with that which occurs

as a manifestation of lateral infarction in intermediate position of the heart. Differentiation may sometimes be made through indirect evidence furnished by (1) the QRS pattern in Lead aV_R, (2) the direction and contour of the P wave in Lead aV_L, and (3) the nature of the change in the pattern of the P wave and QRS complex in Lead aV_L when the tracing is repeated in a different position and during deep respiration. When the foregoing evidence is inconclusive, supplementary high precordial and axillary leads are indicated.

(1) The vertical position which leads to the transmission of cavity potentials to the left arm generally results in the registration of a comparable QR pattern in Lead aV_R from simultaneous transmission of cavity potentials to the right arm. Thus the RS complex in Lead aV_R in Case 129 was strongly against vertical position, but compatible with the presence of a lateral infarction.

(2) When sinus rhythm is present, the direction and contour of the P wave in Lead aV_L is of considerable indirect aid in determining whether a QR or QS complex is a manifestation of lateral infarction in an intermediate heart or a normal variant associated with vertical or semivertical position. The upright P wave with gently sloping limbs normally found in Leads V_5 and V_6 is due to transmission of the potential variations of the lower part of the left atrium through the lateral wall of the left ventricle to the electrode in the axilla. The registration of an upright P wave in Lead aV_L, which is similar to that in Leads V_5 and V_6, indicates that the potential variations of the left atrium are likewise transmitted through the lateral wall of the left ventricle to the left arm. This constitutes strong indirect evidence that the predominant pathway for the transmission of the potential variations of the left ventricle to the left arm extends from the epicardial surface of the lateral wall and not from the cavity through the mitral orifice. A prolonged Q wave and high Q/R ratio in Lead aV_L, under these circumstances, are diagnostic of lateral infarction.

The inverted and diphasic P wave with precipitous intrinsicoid downstroke normally recorded in esophageal leads from above and behind the left atrium is due to direct transmission of the potential variations of the superior and posterior walls of the left atrium to the nearby electrode. The registration of an inverted to diphasic P wave with a steep downstroke in Lead aV_L indicates transmission of the potential variations of the superior or posterior walls of the left atrium directly to the left arm. When Lead aV_F displays a prominent R wave derived from the posterior wall of the left ventricle, the combination of an inverted to diphasic P wave and QR to QS complex in Lead aV_L suggests that the predominant pathway from the ventricles to the left arm may extend from the endocardial surface through the mitral orifice and left atrium. Under these circumstances, a deep, prolonged Q wave may be found in Lead aV_L, irrespective of the presence or absence of infarction of the free wall of the left ventricle. Further procedures essential to the differential diagnosis are discussed later.

(3) Repetition of Lead aV_L in the erect posture and during deep breathing is advisable when the tracing in the recumbent position reveals an inverted or diphasic P wave and a deep, prolonged Q wave. If such a maneuver produces an upright P wave in Lead aV_L, the nature of the change in the QRS pattern will aid considerably in determining whether the Q wave in the original tracing was

a normal variant or a manifestation of lateral infarction. Disappearance of the Q wave or drastic reduction in its duration to 0.02 second or less and in its amplitude to 25 per cent or less of the succeeding R wave indicates that the Q wave in the original tracing was a normal variant. Persistence of a Q wave over 0.02 second in duration and a Q/R ratio exceeding 25 per cent points toward lateral infarction, as will be exemplified by the findings in Case 142.

(4) Supplementary high precordial leads,[12] taken at the intersections of a horizontal line through the sternal terminus of the third intercostal space with vertical lines in the plane of precordial Positions 3, 4, 5, 6, and 7 are advisable whenever the findings in Lead aV_L are suggestive, but not diagnostic, of infarction. Discussion of these leads has been reserved for a companion manuscript on lateral infarction.[9]

Correlation of Electrocardiographic and Pathologic Findings in Posterolateral Infarction.—The thirty-three cases of posterolateral infarction were classified in accordance with the distribution of the lesion in reference to the long axis of the heart into the following groups: apical one-third, nine cases; middle one-third, one case; apical one-half to two-thirds, five cases; basal one-half to two-thirds, four cases; infarction extending more than two-thirds of the length of the posterolateral wall, fourteen cases. The infarct was confined to the subendocardial half of the wall in eight cases. In the remainder, it was most dense in this layer, but reached the epicardial surface of a portion of the posterolateral wall. The lesion was recent in twelve cases and healed in the other twenty-one. Electrocardiographic studies were made during the acute stage in four of the latter.

The standard leads are not reviewed since separate analyses have shown them inferior to the Goldberger leads in the detection of both posterior and lateral infarction.[8,9] Precordial Leads V_1 through V_4 revealed reciprocal changes in the RS-T complex in eleven of the sixteen patients observed during the acute stage of posterolateral infarction. The presence of acute RS-T depression in these leads or the presence of exceptionally tall R or T waves is sufficient to arouse the suspicion of posterior or posterolateral infarction.

The evidence in Lead aV_F referable to the posterior portion of the infarct was interpreted in accordance with previously described criteria[8] as either diagnostic, borderline to strongly suggestive, or negative. The signs in Leads aV_L, V_6, and V_5 referable to the lateral portion of the infarct were similarly interpreted, according to criteria already described. With these four leads being taken into consideration, the cases have been classified into the following four groups: (1) those with findings suggestive to diagnostic of both aspects of the infarct (ten cases); (2) those with signs of the lateral, but not the posterior, lesion (nine cases); (3) those with evidence of posterior, but not of lateral, infarction (twelve cases); and (4) those with negative findings (two cases).

(1) Leads V_5, V_6, aV_L, and aV_F supplied evidence regarded as diagnostic of both the lateral and posterior aspects of the recent lesion in Cases 124, 126, and 130, and of both aspects of the healed infarct in Cases 96, 129, and 131. The QR pattern was borderline in Case 130 and the diagnosis was established by the associated changes in the RS-T complex. In Case 126, signs of the lateral extension were present in Lead V_6 during the acute stage, but disappeared after

the lesion healed. Evidence diagnostic of the lateral and suggestive of the posterior part of the infarct was found in two other patients with a recent lesion (Cases 125 and 127) and one with a healed lesion (Case 132), and signs suggestive of both parts of the old infarct, but diagnostic of neither, were found in Case 133. In most of the patients with abnormal Q-wave patterns in Leads V_5 and V_6, the lesion continued into the apical third of the anterolateral wall. Occasionally, as in Case 124, abnormal Q waves were found in Lead V_6 and even in Lead V_5, despite the fact that the anterior boundary of the lesion was in the posterior part of the lateral wall. Counterclockwise rotation, together with forward displacement of the apex, probably accounted for the transmission of the potential variations of the infarcted posterolateral wall of the apex to Positions 5 and 6.

(2) The electrocardiogram was strongly suggestive to diagnostic of the lateral portion of the infarct, but negative for the posterior part of the infarct in three patients with a recent lesion and in six with a healed lesion. The absence of signs from Lead aV_F was attributable to horizontal position in five patients (Cases 135, 151, 152, 154, and 159); and to a primary lateral infarct, which involved only the apical third of the posterolateral wall, in three (Cases 142, 145, and 157). Extensive lateral and posterolateral infarction was present in the remaining patient (Case 158), and the normal pattern in Lead aV_F was probably transmitted from the intact posteroseptal portion of the wall.

(3) The electrocardiogram was strongly suggestive to diagnostic of the posterior portion of the infarct, but failed to show QRS changes of lateral infarction in Cases 19, 87, 88, 93, 94, 104, and 128, studied in the acute stage, and in Cases 95, 97, 98, 100, and 134, studied after healing. RS-T patterns suggestive of the ischemic zone were found in Leads V_5, V_6, and/or aV_L in six of the seven patients with a recent posterolateral infarct.

The lesion involved the apical portion of the posterolateral wall in Cases 93, 94, and 100. Incomplete left bundle branch block accounted for the absence of diagnostic signs in Leads V_5, V_6, and aV_L in Case 100. The findings were negative in the other two patients, despite the fact that the infarct continued into the apical portion of the anterolateral wall. This was explained by the presence of marked clockwise rotation. In Case 93, all three leads reflected the potential variations of the transitional zone, whereas in Case 94, Lead V_5 was transitional and Leads V_6 and aV_L reflected the potential variations of the anteroseptal wall of the left ventricle.

Extensive infarction of the basal two-thirds of the posterolateral wall was found in Cases 19, 87, 88, 95, 97, 98, 104, 128, and 134. The failure to detect signs of the lateral portion of the lesion in Lead aV_L of seven of these patients was due to clockwise rotation. The pattern in Lead aV_L of these patients corresponded closely with that in one of the first four precordial leads, indicating that the potential variations of the left arm were transmitted chiefly from the anteroseptal wall of the right or left ventricle. The prominent R wave found in Lead aV_L of the other two patients (Cases 87 and 88) was representative of the pattern customarily attributed to transmission of the potential variations of the lateral wall of the left ventricle to the left arm. This R wave resembled that recorded in Leads V_4 through V_6 and was probably derived from the uninfarcted

anteroseptal wall or apical third of the anterolateral wall. The infarct continued into the apical portion of the posterolateral wall of most of the foregoing nine patients, but failed to involve the apical third of the anterolateral wall. The sparing of this portion of the heart, together with the clockwise rotation, accounted for the absence of abnormal Q-wave patterns in Leads V_5 and V_6.

(4) Neither aspect of the infarct was diagnosed from the standard and unipolar limb leads and precordial Leads V_1 through V_6 in Cases 136 and 137. The failure to recognize the posterior part of the lesion was attributable to horizontal position in both cases. Left bundle branch block obscured signs of the lateral infarct in Case 136. The lesion of the lateral wall was relatively small in Case 137, but might have been recognized, if additional leads had been taken.

From a survey of these and other cases, it would appear that abnormal Q-wave patterns are usually present in Leads V_5 and/or V_6 when the infarct involves the apical third of the anterolateral wall, but not when it involves the apical third of the posterolateral aspect of the left ventricle. Leads V_7 and V_8 may provide evidence of the latter,[1] and should be taken when the routine leads reveal changes suggestive of either posterior or lateral infarction. Extensive infarcts of the basal one-half or two-thirds of the posterolateral wall are not recognizable from Lead aV_L when there is sufficient clockwise rotation so that the pattern in this lead resembles that in one of the first four precordial leads. Under these circumstances, high precordial and axillary leads are indicated and are preferably taken at the intersections of a horizontal line at the level of the sternal terminus of the third intercostal space with vertical lines in the plane of the V_4 through V_7 positions. The posterior portion of an extensive posterolateral infarct is not detectable in Lead aV_F when the heart is rotated counterclockwise into a semihorizontal to horizontal position. If leads in the posterior axillary line are negative or inconclusive in horizontally placed hearts, esophageal leads may be needed to establish or exclude posterior infarction.

SUMMARY

In thirty-three cases of pathologically established posterolateral infarction, electrocardiograms consisting of precordial Leads V_1 through V_6 and the Goldberger and standard limb leads were studied to evaluate the evidence furnished by these leads for the detection and localization of the infarct. The findings in Lead aV_F were employed as an index of the posterior aspect of the lesion and the findings in Leads V_5, V_6, and aV_L were used as an index of the lateral aspect. The interpretation of Lead aV_L has been discussed in detail, whereas the criteria used for the other leads were established in previous reports.

In eleven of the sixteen patients observed during the acute stage, precordial Leads V_1 through V_4 revealed reciprocal depression of the RS-T segment or exaggeration in the height of the R and/or T waves, sufficient to arouse the suspicion of posterolateral infarction. On the other hand, the standard limb leads were much less dependable than the unipolar limb leads and supplied no additional information.

The findings in Leads aV_F, aV_L, V_5, and V_6 were regarded as strongly suggestive to diagnostic of both aspects of the infarct in ten cases; of the posterior, but not the lateral, lesion in nine cases; of the lateral, but not the posterior, lesion in twelve cases; and were negative in the other two cases.

The commonest cause for failure to detect the posterior portion of the infarct in Lead aV_F was counterclockwise rotation into a semihorizontal to horizontal position. However, lesions that involved the posterolateral, but spared the posteroseptal, wall were sometimes not recognizable from Lead aV_F, even though the heart was in a vertical to intermediate position.

The commonest cause for failure to detect evidence of posterolateral infarction in Lead aV_L was clockwise rotation. In nine patients with extensive infarction of the basal portion of the posterolateral wall, the QRS pattern in Lead aV_L resembled that in one of the first four precordial leads, indicating that the potential variations of the left arm were transmitted chiefly from the anteroseptal wall of the right or left ventricle.

Leads V_5 and V_6 seldom yielded abnormal Q-wave patterns unless the posterolateral infarct continued into the apical third of the anterolateral wall. The occasional association of abnormal Q-wave patterns in Lead V_6 or both Leads V_6 and V_5 with infarction of the apical third of the posterolateral wall was attributed to counterclockwise rotation of the heart or anterior displacement of the apex.

Precordial Leads V_1 through V_6, together with the Goldberger and standard limb leads, are inadequate for the accurate localization of posterolateral infarction, but generally reveal sufficient evidence to arouse the suspicion of at least one aspect of the lesion. Under these circumstances, Leads V_7, V_8, and supplementary high axillary leads are indicated to explore the apical and basal aspects, respectively, of the posterolateral wall.

REFERENCES

1. Wilson, F. N., et al.: Precordial Electrocardiogram, Am. Heart J. **27**:19, 1944.
2. Wilson, F. N., Rosenbaum, F. F., and Johnston, F. D.: Interpretation of the Ventricular Complex of the Electrocardiogram, Advances in Internal Medicine **2**:1, New York, 1947, Interscience Publishers.
3. Hecht, H. H.: The Localization of Myocardial Infarcts With Particular Reference to Lateral Infarction and the T_1Q_3 Pattern, Proc. Am. Federation Clin. Research **2**:102, 1945.
4. Myers, G. B., Klein, H. A., and Hiratzka, T.: Correlation of Electrocardiographic and Pathologic Findings in Anteroposterior Infarction, Am. Heart J. **37**:205, 1949.
5. Goldberger, E.: The Differentiation of Normal From Abnormal Q Waves, Am. Heart J. **30**:341, 1945.
6. Myers, G. B., Klein, H. A., and Hiratzka, T.: Correlation of Electrocardiographic and Pathologic Findings in Large Anterolateral Infarcts, Am. Heart J. **36**:838, 1948.
7. Myers, G. B., and Oren, B. G.: The Use of the Augmented Unipolar Left Leg Lead in the Differentiation of the Normal from Abnormal Q Wave in Standard Lead III, Am. Heart J. **29**:708, 1945.
8. Myers, G. B., Klein, H. A., and Hiratzka, T.: Correlation of Electrocardiographic and Pathologic Findings in Posterior Infarction, Am. Heart J. In press.
9. Myers, G. B., Klein, H. A., and Stofer, B. E.: Correlation of Electrocardiographic and Pathologic Findings in Lateral Infarction, Am. Heart J. **37**:374, 1949.
10. Myers, G. B., Klein, H. A., and Stofer, B. E.: Correlation of Electrocardiographic and Pathologic Findings in Anteroseptal Infarction, Am. Heart J. **36**:535, 1948.
11. Myers, G. B., and Klein, H. A.: The Relation of Unipolar Limb Leads to Precordial and Esophageal Leads, Am. Heart J. **35**:727, 1948.
12. Rosenbaum, F. F., Wilson, F. N., and Johnston, F. D.: The Precordial Electrocardiogram in High Lateral Myocardial Infarction, Am. Heart J. **32**:135, 1946.

THE PULMONARY ARTERIAL PRESSURE

S. Rodbard, Ph.D., F. Brown, M.D., and L. N. Katz, M.D.
Chicago, Ill.

IN THE course of an analysis of factors involved in the maintenance of the normal systemic arterial pressure[1,2] we became interested in certain comparative aspects of the pulmonary arterial pressure. For this purpose we have measured the pulmonary arterial pressure in a reptile (turtle) and a bird (chicken) and we have reviewed data previously obtained in a mammal (dog).[3,4,5] These studies suggest that while the systemic arterial pressures may vary widely in the various classes, the pulmonary arterial pressures are remarkably similar in all vertebrates.

METHODS AND RESULTS

Turtle.—Pulmonary and systemic arterial pressures were measured in fourteen turtles (*Pseudemys elegans*) after removal of a circular disc, about 3.0 cm. in diameter, from the plastron overlying the heart and great vessels. The subjacent connective tissue was stripped away to expose the left pulmonary artery and the left aorta. The pressure in the main pulmonary artery was measured with a cannula introduced cardiad into the left pulmonary artery. The systemic pressure as transmitted via the right aorta was determined by means of a second cannula placed peripherad into the left aorta. The cannulas were then attached to the Hamilton manometers[6] for optical registration of the pressure pulses. Heparin was used to prevent clotting.

During ventricular systole the pressures in the pulmonary artery and in the aorta reached essentially similar levels. During diastole, the pulmonary pressure fell away more rapidly and to lower levels than did the aortic. As a result, the pressure in the pulmonary artery at the end of diastole was usually from 10 to 30 mm. Hg lower than that in the aorta. Because of this lower pressure, ejection and the rise in pressure began earlier during the following contraction of the common ventricle in the pulmonary than in the systemic vessels.

The pulse pressure in the systemic circuit was 5 to 10 mm. Hg less than that in the pulmonary artery (Table I) and it was relatively constant and independent of the height of the systemic pressure. For example, in the course of one given experiment, pressures of 35/27 and 19/10 mm. Hg were recorded at separate times.

From the Cardiovascular Department (this Department is supported in part by the Michael Reese Research Foundation), Medical Research Institute, Michael Reese Hospital, and the Department of Physiology, University of Chicago, Chicago, Ill.

Aided in part by a grant from the Department of the Army to the Michael Reese Hospital (Dr. L. N. Katz, the responsible investigator).

TABLE I. PULMONARY AND AORTIC PRESSURES IN THE TURTLE

TURTLE NUMBER	AORTIC PRESSURE*		PULMONARY ARTERIAL PRESSURE	
	SYSTOLIC (MM. HG)	DIASTOLIC (MM. HG)	SYSTOLIC (MM. HG)	DIASTOLIC (MM. HG)
158	42	28	40	10
159	41	29	40	24
160	30	22	30	10
161	30	25	32	8
162	—	—	30	10
174	37	28	35	10
Averages	36	26	35	12

*In this column, — means no record made.

By contrast, the pulmonary pulse pressure was much more variable. The pulmonary diastolic level was almost always below 20 mm. Hg, ranging between 8 and 24 mm. Hg, and averaging about 12 mm. Hg (Table I). Conditions which tended to raise the systemic pressure reflected themselves in the pulmonary circuit primarily by an increase in the *systolic* pressure, but had only a slight effect on the diastolic level. For example, warming the turtle, or the injection of epinephrine, usually elevated the systemic diastolic pressure and the systolic pressures in both circuits by the same amount, but the pulmonary diastolic pressure was little affected.

Dog.—This laboratory has previously used a modified London cannula to measure the pulmonary arterial pressure in the intact unanesthetized dog.[4,5] These experiments have shown the pulmonary arterial pressure to range about 28/10 mm. of mercury. This value was not affected by the induction of systemic nephrogenic hypertension,[4] nor by epinephrine and acetylcholine, agents which markedly affected the systemic pressure.[5] The pulmonary arterial pressure appeared to be affected almost solely by a disparity in the output of the left and right ventricles, thus responding passively, rather than actively, as is the case in the systemic circuit. These results are similar to those of other investigators in the cat[7] and in man.

Chicken.—The pulmonary arterial pressure was measured successfully in six white Leghorn chickens of about 16 weeks of age. The pentobarbitalized animal was placed on its right side and the left wing folded back to expose the thoracic cage. The prominent external thoracic vein can be seen coursing from the angle of the wing in a posteroventral direction. An incision about 2 inches in length was made along this vein, exposing the pectoralis major, which was then separated from the thoracic cage by blunt dissection. The sternal portions of the ribs were removed and the pericardial sac was split, exposing the left pulmonary artery. This vessel was then ligated as close to the lung hilum as possible and cannulated. Much care was necessary at this point because of the fragility of the vessel, especially in young birds. The cannula was attached to the optically recording Hamilton manometer. A typical record is illustrated in Fig. 1.

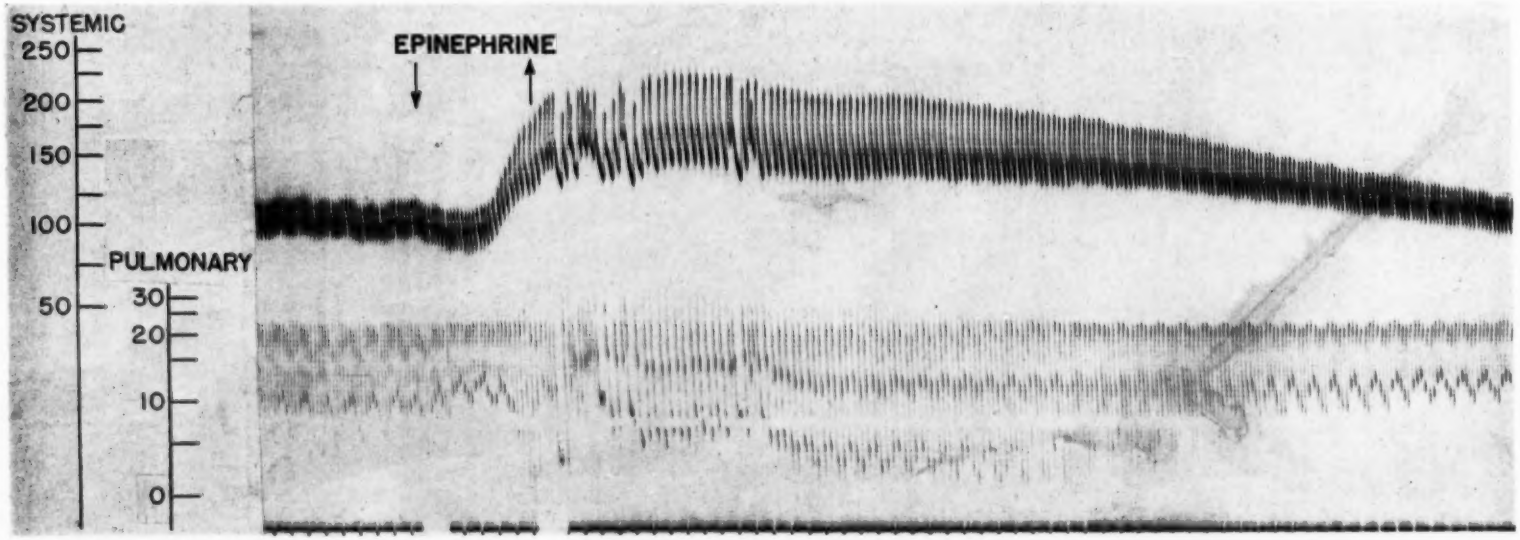


Fig. 1.—The pulmonary and arterial blood pressure in the chicken. Effect of 0.5 mg. of epinephrine. Calibrated in mm. of mercury. Upper curve, systemic arterial pressure. Lower curve, pulmonary arterial pressure. Epinephrine injection given between the arrows. Time is in seconds. Note that epinephrine injection produced a slowing of the heart which was associated with an increase in the systemic arterial pressure, but with no significant change in the mean pulmonary arterial pressure.

The normal pulmonary arterial pressure of the chicken was found to average 23/12 mm. Hg, ranging from 15 to 30 systolic and from 5 to 20 diastolic (Table II). The possibility that the opening of the thorax or the occlusion of the left pulmonary artery may have introduced errors into the measurement must be mentioned. Obstruction of the left pulmonary artery would, if anything, have tended to increase the pulmonary arterial pressure. However, results on animals, including man, show that neither opening of the pleura to atmospheric pressure nor occlusion of one major branch of the pulmonary artery significantly alters the pressure in the main pulmonary artery.[7]

TABLE II. PULMONARY ARTERIAL PRESSURE IN THE CHICKEN

CHICKEN NUMBER	SYSTOLIC PRESSURE (MM. HG)	DIASTOLIC PRESSURE (MM. HG)	HEART RATE (PER MINUTE)	RESPIRATORY RATE* (PER MINUTE)
1	32	20	276	60
2	26	10	260	36
3	18	7	380	48
4	18	8	240	—
5	31	20	282	48
6	17	10	318	51
Averages	24	12	293	49

*In this column, — means no record made.

The systemic blood pressure, recorded from the sciatic artery ranged from 130/100 to 90/75 mm. of mercury. These values, lower than those found in unanesthetized intact birds,[1] may have been the result of the trauma produced by the surgery or of the action of the anesthetic on the circulation and on body temperature.

Injection of 1.0 mg. of epinephrine into the sciatic vein resulted in a rise in systemic pressure of 40 to 80 mm. Hg; the pulmonary arterial pressure was affected only slightly with occasional rises of up to 5.0 mm. Hg followed by a fall of this magnitude (Fig. 1). As in the dog, these appeared to represent passive changes resulting from changes in heart rate and backward transmission of the effect of the vasoconstrictor agent on the systemic circuit and from variations in venous return during recovery from systemic vasoconstrictuion.

DISCUSSION

The fact that the pressure in the artery to the respiratory apparatus (respiratory arterial pressure) is essentially of the same order in three different classes of vertebrates suggested that it would be of value to consider more generally some comparative aspects of the lesser circulation. These are represented schematically in Fig. 2. Only physiological situations are discussed; pathological variations will be taken up in a later communication.

The functional equivalent of the pulmonary circulation in the fish is seen in the gill circulation, in which the process of oxygenation of the blood and loss of

carbon dioxide is accomplished. The few blood pressures which have been recorded in the fish show the pressure to be about 30 mm. Hg in the ventral aorta (pulmonary) and about 23 mm. Hg in the dorsal aorta (systemic).[8-12] In the passage of the blood through the low-resistance gill capillaries and the collection of the oxygenated blood into the dorsal aorta, the pressure is necessarily somewhat reduced. The gill capillaries apparently impose little resistance to flow.[8] In this primitive type of cardiovascular system, the pressure in the ventral aorta (respiratory) is slightly higher than that in the systemic circu-

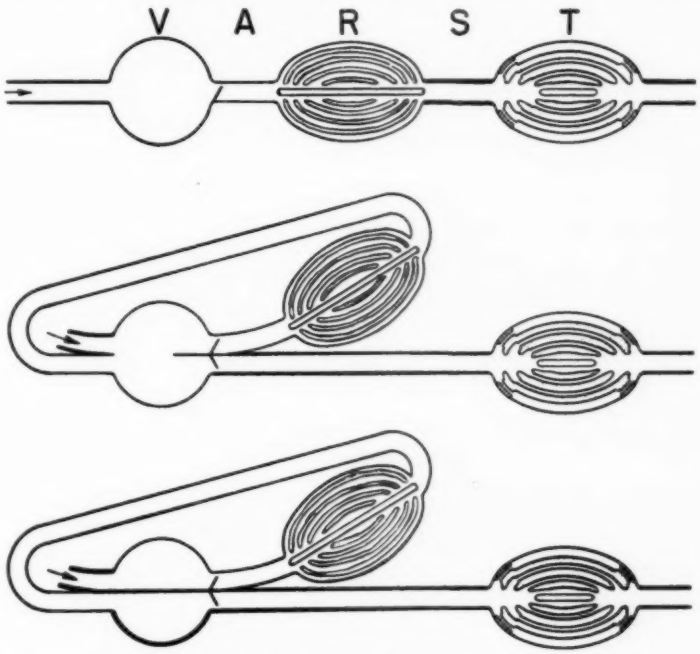


Fig. 2.—A schematic representation of the relation between the pulmonary and systemic pressures in the fish (upper diagram), amphibiae and reptiles (middle diagram), and mammals and birds (lower diagram). At the left, the arrow indicates the route of the venous return from the systemic circuit. Under *V* is placed the ventricle(s); under *A* is the artery to the respiratory organ; under *R* is the respiratory organ, either gill or lung; under *S* is represented the systemic aorta; and under *T* is placed the systemic organs with various types of vasomotor action in the several parallel circuits. The design of *R* suggests the low-resistance circuit of the homogeneous respiratory organ. The design of *T* suggests the means by which blood is redistributed to heterogenous parts of the systemic circuit. Low-resistance shunts (center) are parallel with progressively vasoactive shunts and a sinusoid-type shunt at the periphery.

lation represented by the dorsal aortas (Fig. 2). Irving[11] remarks that perfusion pressures higher than 35 mm. Hg were not practicable since the thin-walled ventral aorta distended excessively under such abnormal conditions. As a result of its position in the vascular tree, the respiratory organ is thus seen as a limiting factor in the level of the systemic pressure which can be attained in the fish.

The next major step in the evolution of the respiratory equipment is exemplified in the development of the pulmonary and cutaneous vasculature in the amphibiae. The systemic arterial pressure has been measured in these

animals and found to be of the same order as that seen in the turtle for the same body temperature.[13,14] The general similarity of the circulation in the amphibiae and the reptiles makes it likely that their circulations operate on similar principles. In the reptiles, the cutaneous respiratory circulation is lost, and the interventricular septum is better developed, but the ventricle still acts essentially as a single chamber. The systemic and pulmonary *systolic* pressures are equal. However, the diastolic pressure in the systemic circuit is definitely higher than in the pulmonary system. As a result, the *mean* systemic pressure is placed at higher levels than the mean pulmonary pressure. This is accomplished by the action of the spiral valve in the pulmonic-aortic trunk which, during diastole, prevents the regurgitation of blood from the higher pressure of the systemic circuit into the pulmonary artery.

Minor adjustments in the output through the systemic and pulmonary circuit may occur since Woodbury and Robertson[15] have suggested that after hemorrhage the orifice of the pulmonary artery may be closed during the greater part of systole. This may effectively reduce the pulmonary output and divert more blood to the systemic circuit. Despite this, the maximal pressure generated in the systemic circuit is still limited by the fact that ejection of blood from a single ventricle cannot effectively increase the systemic output without increasing the pulmonary output to an even greater extent. An increase in the systolic pressure must therefore result in a greater diversion of blood into the pulmonary circuit and cannot but contribute to a decreased efficiency of the heart beat as far as the systemic pumping action is concerned. At higher body temperatures and therefore at higher oxygen need, an increasing systolic pressure probably would act to increase the pulmonary flow at a greater rate than that being supplied to the aorta. In this way, the small respiratory surface area of the amphibian and reptilian lung may be partially compensated.

An interesting problem which has faced physiologists interested in the pulmonary circulation has been the remarkable insensitivity of the pulmonary circulation to the action of agents which markedly affect the systemic circuit. A plausible explanation of this unexpected refractoriness of the pulmonary vasculature may lie in its phylogenetic derivation and in the homogeneity of its structure. Thus it can be easily appreciated that in the fish an increase in resistance in the gill arterioles would markedly increase the work of the heart, but would provide no useful function in the gill circuit, since, if valuable filtrable elements of the plasma are not to be lost into the surrounding medium, the pressure must be reduced to levels which do not force a transudate through the respiratory capillaries. The utility of vasoactive substances and vasomotor reflexes apparently lies in the redistribution of blood flow from one to another portion of the heterogeneous systemic circuit. Thus muscular activity leads to vasodilation of the arterioles of the muscles and a consequent increase in blood flow to the active parts. Compensatory vasoconstriction in other parts of the systemic circuit occurs and prevents the fall in blood pressure which otherwise would develop. The homogeneity of the pulmonary circuit would appear to require no preferential shunting of blood in the lungs. In this system, the presence of active arterioles could act only to increase the load on the ventricle without accomplishing any useful function.

In the case of the common ventricle of the amphibiae and reptiles, pulmonary arteriolar vasoconstriction could act only to decrease the blood flow through the lungs and handicap the gaseous exchange in the lungs and lead toward anoxemia.

The division of the reptilian single-chambered ventricle into two separate chambers occurs in the homeothermic mammals and birds and accomplishes the separation of the arterialized from the venous blood. Of equal importance, it makes possible an increase in the systemic pressure without an equal increase in the pulmonary pressure.

The fact that at least three different groups of reptiles have developed a four-chambered heart has made it possible to compare certain features of the circulation and draw some general conclusions. The crocodiles apparently have maintained the pressure relationship seen in the turtle, with systemic pressures essentially of the same order as those in the lower reptiles.[16] The presence of a large ductus arteriosus in these animals makes it likely that the pulmonary pressure is at similarly low levels. Mammals and birds, evolving from widely separated reptilian forebears, have developed body temperatures and systemic arterial pressures at different levels,[17] but have evidently proceeded in a generally similar manner with regard to the level of the pulmonary arterial pressure. In mammals, body temperatures range about 37°C. with systemic diastolic pressures of about 80 mm. of mercury. Birds, with body temperatures about 42°C., have systemic diastolic pressures of about 120 mm. of mercury.[10] However, the pulmonary arterial pressures in both groups of animals are about 25/10 mm. Hg, and this level, of course, is generally similar to that found in the pulmonary artery in the cold-blooded vertebrates.

The course of development of the circulation in the vertebrates is thus seen to involve the escape of the systemic circulation from the limitations placed upon it by the low-resistance pulmonary circuit. In the fish these circuits are in series, with the respiratory apparatus between the single ventricle heart and the systemic circulation. The assumption of terrestial life was unquestionably facilitated by the development of the systemic circulation parallel with the pulmonic (Fig. 2), which permitted a significant but limited increase in the mean systemic pressure.

The cutaneous respiratory circulation is lost in the reptiles, but the incomplete separation of the ventricles marks no fundamental hemodynamic change. Similarly, the incomplete separation of the circulations seen in the crocodilia and in prenatal mammals and birds places limitations on the level to which the systemic pressure can be raised because of the low-resistance pulmonary shunt. The complete division of the ventricles in the homeotherms eliminates this effect and permits the systemic pressure to be raised independently of the pressure in the respiratory circuit. The final disappearance of shunts between the venous and arterial circulations (ductus arteriosus and foramen ovale) provides the pumping equipment for the increase in blood pressure without undue loss of efficiency of the heart, and makes possible a vascular apparatus capable of meeting the increased circulatory demands placed by the high metabolic rates of warm-blooded animals.

Probably the most significant factor limiting the level of the pulmonary arterial pressure is the low resistance to flow of blood through the respiratory apparatus. This in turn depends on the primary function of the respiratory

capillaries, which is the exchange of gases with the environment. Such capillaries, if they are to permit the rapid passage of oxygen and carbon dioxide, must be thin and in close contact with the external environment. For greatest efficiency they require a rapid flow of blood and a large surface area exposed to the environment. Further, the pressure must be lower than the oncotic pressure of the blood so that no significant transudate is produced. These conditions all conspire to maintain a low pulmonary arterial pressure.

The marked distensibility of the pulmonary capillaries, surrounded by air and unsupported by tissues, permits large increases in volume and thus prevents a significant pressure change during ventricular ejection. The fact that the mean pulmonary arterial pressure is probably only about 14 mm. Hg and the capillary pressure, about 10 mm. Hg makes possible the osmotic reabsorption during diastole of transudate which might pass through the capillary wall during the momentary heightened pressure of systole.

By their tremendous distensibility, the pulmonary capillaries furnish a buffer between right and left ventricles. Thus, the output of the left ventricle may, for brief periods, be less than the output of the right ventricle. No increased pulmonary pressure and, therefore, no increased transudate and edema occur until the storage capacity of the lungs, as indicated by a markedly reduced vital capacity, is encroached upon.

If the respiratory arterial pressure were to be raised significantly, the respiratory capillary epithelium would begin to function in a fashion similar to that of the renal glomerulus. In the fish this would lead to rapid dehydration and salt loss, while in the terrestial animal, the accumulation of transudate on the pulmonary epithelium would impede gas diffusion and produce hypoxia, or if severe, would lead to frank pulmonary edema. In any event, the development of conditions permitting a significant increase in the respiratory capillary pressure would act as a lethal variant.

By contrast, the systemic capillaries are supported and surrounded by the tissues, and the production of transudate by an increased pressure automatically increases the tissue pressure and results in an increased return of such fluid to the circulation via the venous system or the lymphatics.

The respiratory arterial pressure is thus seen to be conservative throughout its history. On the other hand, the metabolic demands for an increased perfusion of the highly active tissues of the homeotherms have been met by the production of a higher head of pressure in the systemic circuit which was made possible by the escape of the systemic circuit from the pressure limitations placed upon it by the pulmonary circuit. However, this development opened the way for an unbridled increase in the level of the systemic arterial pressure which in some cases may be more than can be borne without injury to the heart and the vascular tree.

SUMMARY

Measurements of the systemic and pulmonary arterial pressure in a reptile (turtle), mammal (dog), and bird (chicken) were used as a basis for a study of the comparative physiology of the lesser circuit. Data on the ventral aortic (pul-

monary) pressure in the fish were available in the literature. In all these the pulmonary arterial pressure was low, ranging around 25/10mm. of mercury. However, the systemic arterial pressure varies markedly from class to class. In the fish, the systemic pressure is lower than that in the gill arteries. In the turtle, the systolic pressures are equal in both circuits, but the systemic diastolic is higher than the pulmonic diastolic pressure; therefore, the mean systemic pressure is also higher. In the homeotherms, the systemic pressure is much higher than in the pulmonary circuit.

The pulmonary arterial pressure remains low in the higher vertebrates, probably as a result of factors which act to increase the rate of exchange of blood gases with those of the environment. These include: (a) the enormous pulmonary vascular bed, (b) the absence of tissue support of the pulmonary capillaries which are exposed over nearly their entire surface to the environment, resulting in (c) the great distensibility of the capillaries permitting little increment in pressure with greatly increased volume. An increased pressure in such a capillary would produce a transudate and result in disturbed respiratory function.

The complete division of the primitive ventricle into two chambers resulted not only in the separation of arterial from venous blood, but also provided conditions in which the systemic pressure could be raised without directly affecting the pulmonary blood pressure and blood flow.

We wish to acknowledge our indebtedness to Dr. A. Surtshin and to Miss L. Taylor for technical assistance in the early phases of this study.

REFERENCES

1. Rodbard, S., and Tolpin, M.: A Relationship Between Body Temperature and the Blood Pressure in the Chicken, Am. J. Physiol. **151**:509, 1947.
2. Surtshin, A., Rodbard, S., and Katz, L. N.: Inhibition of Epinephrine Action in Severe Hypoxemia, Am. J. Physiol. **152**:623, 1948.
3. Johnson, V., Hamilton, W. F., Katz, L. N., and Weinstein, W.: Studies on the Dynamics of the Pulmonary Circulation, Am. J. Physiol. **120**:624, 1937.
4. Katz, L. N., and Steinitz, F.: Pulmonary Arterial Pressure in Experimental Renal Hypertension, Am. J. Physiol. **128**:433, 1940.
5. Katz, L. N., and Friedberg, L.: The Effect of Drugs on the Pulmonary and Systemic Arterial Pressure in the Trained Unanesthetized Dog, J. Pharmacol. & Exper. Therap. **77**:80, 1943.
6. Hamilton, W. F., Brewer, G., and Brotman, I.: Pressure Pulse Contours in the Intact Animal, Am. J. Physiol. **107**:427, 1934.
7. Alberti, V. A. J.: La Presion de la Arteria Pulmonar, Buenos Aires, 1948, El Ateneo.
8. Schoenlein, V., and Willem, K.: Beobachtungen über Blutkreislauf und Respiration bei einigen Fischen, Ztschr. f. Biol. **32**:511, 1895.
9. Bruenings, W.: Zur Kreislaufs der Fische, Arch. f. d. ges. Physiol. **75**:599, 1899.
10. Woodbury, R. A., and Hamilton, W. F.: Blood Pressure Studies in Small Animals, Am. J. Physiol. **119**:663, 1937.
11. Irving, L., Solandt, D. Y., and Solandt, O. M.: Nerve Impulses From Branchial Pressure Receptors in the Dogfish, J. Physiol. **84**:187, 1935.
12. Burger, J. W., and Bradley, S. E.: Some Data on Aortic Blood Pressures in the Dogfish, *Squalus acanthus*, Anat. Rec. **99**:670, 1947.
13. Schulz, F. N.: Studien über das Verhalten des Blutdrucks von *Rana esculenta* unter den verschiedenen aussern Bedingungen, insbesondere bei verschiedener Korpertemperatur. Arch. f. d. ges. Physiol. **115**:386, 1906.
14. Rodbard, S.: Unpublished data.
15. Woodbury, R. A., and Robertson, G. G.: The One Ventricle Pump and the Pulmonary Arterial Pressure of the Turtle, Am. J. Physiol. **137**:628, 1942.
16. Soetbeer: Quoted in Schulz.[13]
17. Rodbard, S.: Body Temperature, Blood Pressure, and Hypothalamus, Science **108**:413, 1948.

PLASMA HEXOSAMINE LEVELS IN ACUTE RHEUMATIC FEVER

CONRAD ROSENBERG, M.D., AND BENJAMIN SCHLOSS, PH.D.
NEW YORK, N. Y.

IN HUMAN plasma there is present a substance which has many of the properties of a polysaccharide. Present evidence, in part based on the work of Rimington,[1] of Bierry,[2] and of Hewitt,[3] suggests that this material is composed of three sugars, mannose, galactose, and glucosamine, and further, that this polysaccharide is chemically bound to the various globulins and to some fractions of the albumin. This polysaccharide appears to be present in plasma concentrations of about 300 mg. per cent. The relatively high concentration, coupled with the fact that plasma polysaccharide has been reported to increase in a wide diversity of pathologic conditions, indicates that it may play an important role in human physiology. Nothing, however, is known about its function, origin, or fate.

No method is available for the direct determination of this substance. Various methods have been developed for estimating the total polysaccharide by the determination of one or more of its components, and the colorimetric methods of Tillmans and Philippi[4] and of Elson and Morgan[5] have had widest application. In the former, mannose and galactose are determined, and in the latter, hexosamine.* One of the limitations of the methods now in use is the uncertainty regarding the quantitative relation of these sugars to the total plasma polysaccharide. A second limitation is that these are colorimetric methods which depend on chemical reactions, the nature of which is still unknown.

Several observers have demonstrated that alterations take place in plasma polysaccharide levels in disease states. West and Clarke[6] made a survey of serum hexosamine levels in a wide variety of conditions and reported values elevated above the normal in sera of patients with infectious diseases, malignancies, and sterile infarcts. In the course of their study they examined single samples of serum of seven patients with rheumatic fever and found that the serum hexosamine ranged from 125 to 184 mg. per cent, while the values determined in twenty-one normal individuals were 76 to 110 mg. per cent.

It has long been known[7,8] that if the sera of patients with pneumonia were innoculated with pneumococci and then incubated, a precipitate appeared,

---

From the Department of Therapeutics, New York University College of Medicine.

This work was made possible in part by funds provided by the Committee for the Promotion of Medical Research, Inc.

*The term "hexosamine" refers here to the naturally occurring amino sugars, glucosamine and galactosamine. Since the methods currently in use fail to distinguish between these two, the more general term hexosamine is used.

whereas in sera of normal persons either no precipitate or only a faint turbidity resulted. Friedemann and Sutliff[9] concluded, as a result of acid titration studies, that it was the presence of an increased amount of polysaccharide that was responsible for this phenomenon and that the increased lactic acid formation that resulted from fermentation of this polysaccharide precipitated the plasma proteins. They further concluded that this polysaccharide present in patients with pneumonia was fermented by pneumococci and thereby differed from the polysaccharide normally present which was not metabolized by the microorganisms. In addition, they were able to demonstrate that this phenomenon was not restricted to patients with pneumonia, but also could be shown to occur in sera of patients with other acute infections, with tuberculosis, and during the course of many normal pregnancies. Youngner,[10] using this method of pneumococcal fermentation and resultant precipitate formation for estimating the amount of polysaccharide present, concluded that there was a relationship between the erythrocyte sedimentation rate and plasma polysaccharide levels in a group of diseases studied. This group included rheumatic fever, tuberculosis, pneumonia, malignancies, and coronary occlusion. Seibert and associates,[11,12] studying individuals with tuberculosis, determined polysaccharide levels and electrophoretic plasma protein patterns. The increase in gamma globulin seen in minimal tuberculosis they felt was indicative of antibody formation, but the rise in the α_2 globulin and polysaccharide that occurred in advanced tuberculosis and carcinoma they suggested might represent tissue destruction.

It is apparent, then, that several workers have observed an increase in the polysaccharide in a wide variety of diseases. It seemed worth extending the investigation of West and Clarke to include a series of successive observations on plasma hexosamine levels in individual patients with rheumatic fever from the onset of the acute phase through the period of convalescence. In this manner, one might determine whether there were any similarity in the pattern demonstrated by different individuals with rheumatic fever, whether or not there were any relationship between the degree of polysaccharide elevation and the severity of the disease, and last, whether there were any correlation between the polysaccharide level and the erythrocyte sedimentation rate.

MATERIAL AND METHODS

The patients with active rheumatic fever reported herein were hospitalized either on the Third Medical Service or the Pediatric Service of Bellevue Hospital.

The seventy-six individuals whose hexosamine levels were taken to represent the normal range included thirty-five who were attending a follow-up cardiac clinic and were being treated for either potential, or possible and potential heart disease. None were included in whom there was any question of recent rheumatic activity. The remaining forty-one normal subjects included students, laboratory technicians, well children who were in the hospital as "boarders," and elderly patients with residual hemiplegias who were awaiting transfer to a hospital for chronic care. There was no significant difference in either the range or the mean value of hexosamine in these two groups.

The laboratory data were obtained from the hospital records, except for the hexosamine values. These were obtained by a modified Elson and Morgan method developed by one of the authors.[13] All determinations were performed in duplicate, and the difference between duplicate runs was 2 per cent or less. Recovery experiments were frequently performed on samples of blood from normal persons and rheumatic fever patients and the added glucosamine was found to be quantitatively determined.

The erythrocyte sedimentation rate was determined on the adult service, by the method of Wintrobe and Landsberg, in Cases F.D., C.D., J.G., S.H., R.J., J.K., A.K., M.M., M.R., and S.S. On the pediatric service the Cutler method was used in Cases J.C., A.D., L.D., R.H., J.K., R.K., T.M., E.P., C.S., G.S., and A.Z.

PRESENTATION OF DATA

The plasma hexosamine level in seventy-six normal individuals ranged from 77 to 113 mg. per cent, lying between 80 and 105 mg. per cent in 92 per cent of this group. The mean value was 92 mg. per cent. Twenty-one patients with active rheumatic fever were studied. Their hexosamine levels together with their sedimentation rates are shown in Fig. 1. The onset of illness was arbitrarily established as that date upon which the patient first noted fever, malaise, joint pain, chest pain, or any of the signs and symptoms of rheumatic fever. The onset was not the day of admission as the patients frequently remained at home for several days or even weeks before coming to the hospital. For this reason, hexosamine levels at the very onset of the attack were rarely determined.

The pattern in active rheumatic fever was quite similar in many of the cases studied and was characterized by an elevation during the onset of the attack and then a return, sometimes very abrupt, to normal levels. This is shown in Fig. 2, which was derived by grouping of all the hexosamine determinations obtained in the twenty-one cases of active rheumatic fever into successive ten-day periods starting with the onset of the disease. The average value was then calculated for each of these ten-day periods and this level was plotted against the midpoint of each of these ten-day periods.

When the plasma hexosamine levels were correlated with the clinical course it was observed that patients with severe attacks of rheumatic fever, as judged by the height and duration of the fever and the intensity of the arthritis or carditis, demonstrated higher hexosamine elevations than those with mild episodes. It was also noted that manifestations of arthritis or carditis sometimes persisted after the hexosamine level had returned to normal. One such case is presented in detail in Fig. 3. On the forty-fifth day of illness the hexosamine level was at the upper limits of normal and remained so although for an additional forty-five days low-grade fever persisted and joint pains recurred whenever salicylates were stopped.

When the convalescent period was complicated by a second episode of rheumatic fever, there was a rise in the plasma hexosamine. Case A. D. (Fig. 1) was admitted with rheumatic polyarthritis and on the fifty-third day, during convalescence, the onset of chorea was noted. This was not accompanied by a change in

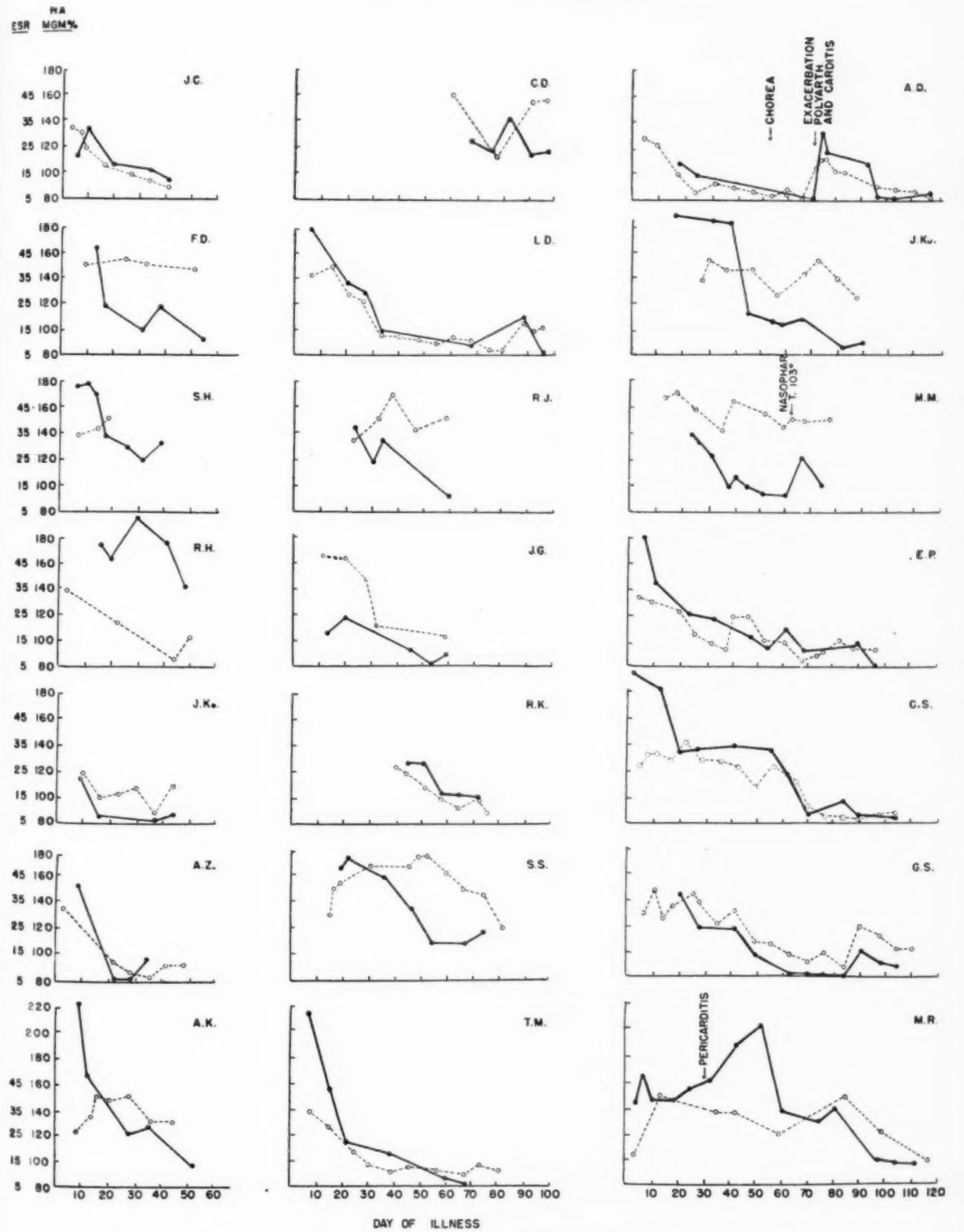


Fig. 1.—Plasma hexosamine levels (solid line) and erythrocyte sedimentation rates (broken line) in twenty-one cases of active rheumatic fever.

the hexosamine level. On the seventieth day, the patient manifested signs and symptoms of carditis and a renewal of the polyarthritis. On this day the hexosamine level was 80 mg. per cent. Two days later, it was 106 mg. per cent, and two days after that it had risen to 130 mg. per cent. Another patient, demonstrating an additional rise in hexosamine accompanying an exacerbation of rheumatic fever, is Case M.R. presented in Fig. 4. In this patient, with an onset of pericarditis, the already elevated hexosamine rose to still higher levels.

The erythrocyte sedimentation rate and the plasma hexosamine parallel each other during most of the period of illness in ten of the twenty-one patients studied (Cases J.C., A.Z., L.D., R.K., T.M., A.D., E.P., C.S., G.S., and M.R.). In the remaining eleven patients there is either a negative or no apparent correlation or the data are too inadequate or too inconclusive to warrant any comparison.

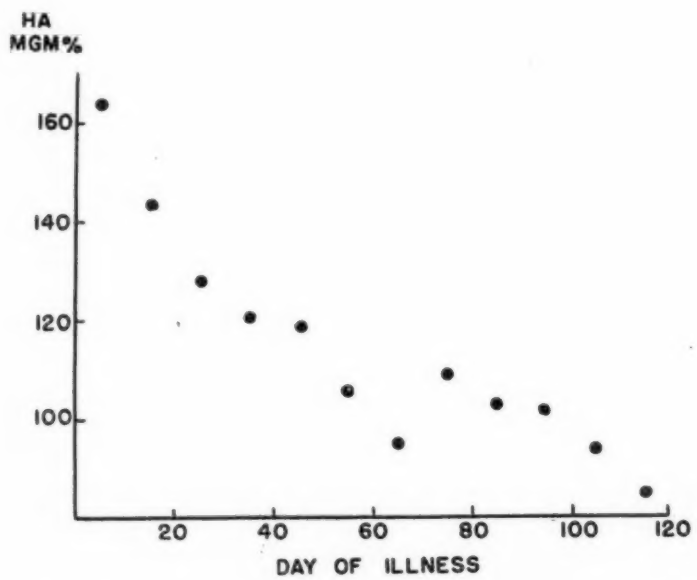


Fig. 2.—The points represent the average of all the plasma hexosamine levels in the twenty-one cases of active rheumatic fever after these levels had been grouped into successive ten-day periods starting with the onset of the illness.

Case M.M. (Fig. 1) developed a nasopharyngitis during the convalescent period and demonstrated a rise in the hexosamine with no evidence of renewed rheumatic activity. As had been mentioned, elevations in plasma hexosamine are not specific for rheumatic fever.

In addition to the twenty-one patients presented in Fig. 1, three patients with chorea alone and two patients with the end stage of rheumatic heart disease who died in congestive failure without clinical evidence of rheumatic activity (no post-mortem examination) demonstrated no elevation in their plasma hexosamine level.

Similar to the observations of West and Clarke,[6] the plasma hexosamine was found to be elevated in a wide variety of illnesses (Table I). High levels were observed in acute pyelonephritis, pneumonia, gonococcal arthritis, subacute bacterial endocarditis, pulmonary tuberculosis, rheumatoid arthritis, multiple myeloma, and myocardial infarction.

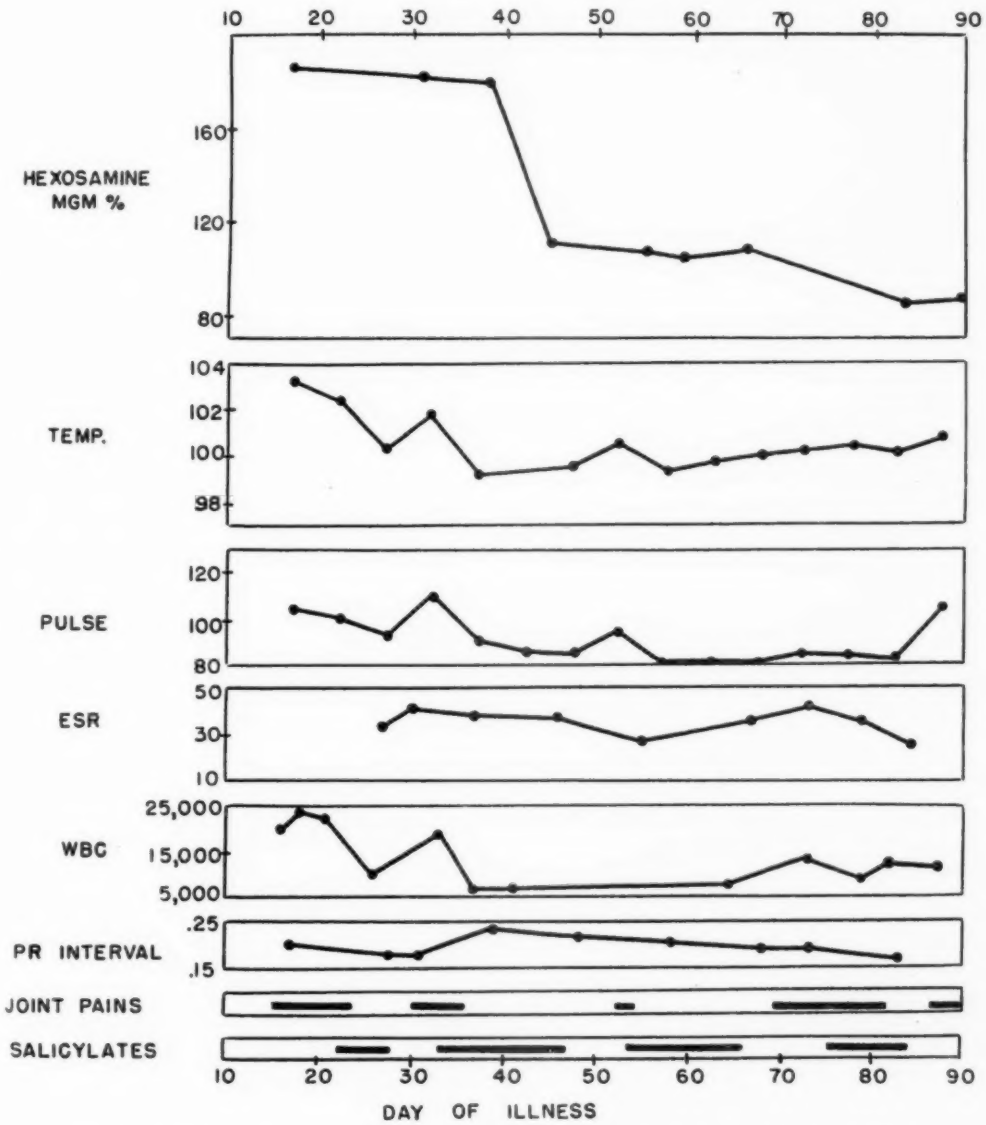


Fig. 3.—A 68-year-old man (J. K.) with a past history of rheumatic fever who was admitted to the hospital with fever and pain in right shoulder and right hip.

DISCUSSION

It is apparent, then, that in a multitude of diseases there is an elevation in the plasma hexosamine and presumably in the plasma polysaccharide. Regardless of the diversity of the offending agent, be it bacteria, sterile infarction, or malignancy, a similarity of response is evoked, namely, a rise in this substance. Its presence in the blood in increased amounts in such a wide variety of diseases suggests that part of the fundamental histochemical response of the body to

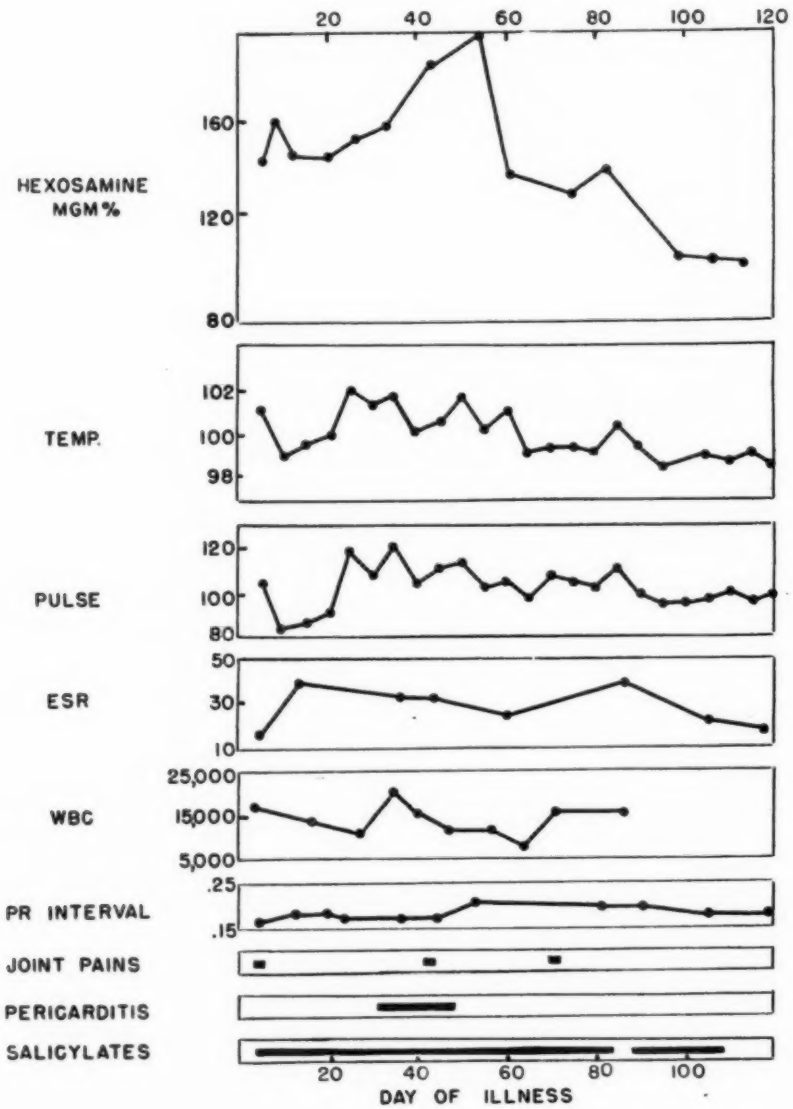


Fig. 4.—A 13-year-old boy (M. R.) with a past history of rheumatic fever and known rheumatic heart disease who was admitted to the hospital with fever and polyarthritis and subsequently manifested a pericarditis with marked effusion.

TABLE I. PLASMA HEXOSAMINE LEVELS IN DIFFERENT ILLNESSES

ILLNESS	HEXOSAMINE (MG. PER CENT)
Acute pyelonephritis	141, 165, 176, 124
Pneumonia	143, 144, 140
Pneumonia	138, 212
Pneumonia	122, 112, 107
Gonococcal arthritis	174
Gonococcal arthritis	134, 156, 142, 126
Gonococcal arthritis	107, 143, 145, 143
Subacute bacterial endocarditis	126, 141, 100, 77, 90
Pulmonary tuberculosis	130
Pulmonary tuberculosis	149
Pulmonary tuberculosis	170
Pulmonary tuberculosis	163
Rheumatoid arthritis	117
Rheumatoid arthritis	167
Multiple myeloma	148, 170
Myocardial infarction	70, 116, 122, 123, 97, 117, 116, 92

Each diagnosis represents an individual patient. The values opposite the diagnosis represent samplings taken during the illness in chronological order from left to right.

injury may be intimately connected with polysaccharide metabolism. It is known that polysaccharides are an important constituent of connective tissue. This, together with the frequency with which alterations in connective tissue occur in disease, suggests that the increased polysaccharide in plasma may be a reflection of the connective tissue response to disease. The data obtained from the twenty-one cases of rheumatic fever studied show that the highest polysaccharide levels were obtained during the early days of the more severe attacks. It may be that the degree and duration of polysaccharide increase is related to the mass of tissue involved in the rheumatic episode and the intensity of its involvement.

SUMMARY

Plasma hexosamine levels were followed in twenty-one patients with acute rheumatic fever, three patients with chorea, and two without clinical evidence of rheumatic activity who died in congestive failure with long-standing rheumatic heart disease. The plasma hexosamine was observed to be elevated in all twenty-one cases of acute rheumatic fever. The usual pattern was an elevation during the early portion of the episode and then a return to normal, which in several cases was very abrupt. The degree of elevation was greater in the severe cases than in the mild ones. In the three patients with chorea and in the two who died in congestive failure without clinical evidence of rheumatic activity, the hexosamine levels were normal. The erythrocyte sedimentation rate and the plasma hexosamine level roughly paralleled each other in ten of the twenty-one cases studied. In confirmation of the work of others, the plasma hexosamine elevation was not found to be specific for rheumatic fever and was observed to be increased in subacute bacterial endocarditis, pulmonary tuberculosis, pneumococcal pneu-

monia, acute pyelonephritis, gonococcal arthritis, rheumatoid arthritis, multiple myeloma, and myocardial infarction.

It is suggested that the increased plasma polysaccharide seen in this variety of diseases reflects a fundamental histochemical response to injury.

The authors wish to express their appreciation to Dr. Maxwell Schubert for his valuable comments and to Julia Morrison Einbinder for her technical assistance.

REFERENCES

1. Rimington, C.: (a) The Carbohydrate Complex of the Serum Proteins, Biochem. J. **25**:1062, 1931.
   (b) Seromucoid and the Bound Carbohydrate of the Serum Proteins, Biochem. J. **34**:931, 1940.
2. Bierry, H.: Sur la nature du sucre protéidique dans le plasma sanguin du cheval, Compt. rend. Soc. de biol. **99**:1837, 1928.
3. Hewitt, L. F.: The Polysaccharide Content and Reducing Power of Proteins and of Their Digest Products, Biochem. J. **32**:1554, 1938.
4. Tillmans, J., and Philippi, K.: Ueber den gehalt der wichtigsten Proteine der Nahrungsmittel an Kohlehydrat und über ein kolorimetrisches Verfahren zur quantitative Bestimmung von sticksstoffreiem Zucker in Eiweiss, Biochem, Ztschr. **215**:36, 1929,
5. Elson, L. A., and Morgan, W. T. J.: A Colorimetric Method for the Determination of Glucosamine and Chondrosamine, Biochem. J. **27**:1824, 1933.
6. West, R., and Clarke, D. H.: The Concentration of Glucosamine in Normal and Pathological Sera, J. Clin. Investigation **17**:173, 1938.
7. Rosenow, E. C.: Studies in Pneumonia and Pneumococcus Infection, J. Infect. Dis. **1**:280, 1904.
8. Longcope, W. T.: A Note Upon the Growth of Pneumococci and Streptococci in Blood Serum, J. Exper. Med. **7**:626, 1905.
9. Friedemann, T. E., and Sutliff, W. D.: Appearance of Fermentable Polysaccharide in the Blood and a Simple Method for Its Detection, Science **90**:335, 1939.
10. Youngner, J. S.: Relation of Sedimentation Rate to Amount of Precipitate Formed in Plasma by Type III Pneumococcus, Proc. Soc. Exper. Biol. & Med. **56**:18, 1944.
11. Seibert, F. B., Nelson, J. W., and Seibert, M. V.: Correlation of Extent of Tuberculosis With Amount of Polysaccharide in the Serum, Proc. Soc. Exper. Biol. & Med. **52**:219, 1943.
12. Seibert, F. B., Seibert, M. V., Atno, A. J., and Campbell, H. W.: Variation in Protein and Polysaccharide Content of Sera in the Chronic Diseases, Tuberculosis, Sarcoidosis, and Carcinoma, J. Clin. Investigation **26**:90, 1947.
13. Schloss, B.: Unpublished data.

AN IMPROVED METHOD FOR VISUALIZING THE CORONARY ARTERIES AT POST MORTEM

R. W. Scott, M.D., A. F. Young, M.D., H. A. Zimmerman, M.D., and Ileen Kroh, B.S.

Cleveland, Ohio

FROM the virtual inception of the study of anatomy, investigators have attempted to further their knowledge of the coronary circulation. As pointed out by Schlesinger,[1] the methods used fall into several categories as follows: (1) careful anatomical dissection; (2) injection of the coronary arteries with various substances such as agar and gelatin, and subsequent clearing of the heart muscle; (3) injection of the coronary arteries with material such as lead, and subsequent digestion of the heart muscle so as to leave a cast of the coronary artery bed; and (4) injection of the coronary arteries with radiopaque material and their study by roentgenograms to demonstrate the arterial tree.

An analysis of these techniques reveals the following disadvantages: (1) Information gained by gross dissection of the coronary arteries obviously is limited to macroscopic vessels and throws no light on the terminal ramifications of the coronary bed. (2) Methods of injection and subsequent clearing of the heart muscle by digestion preclude the histologic study of the myocardium as well as careful observations of the valve leaflets, orifices, and endocardium. (3) Roentgenographic studies prior to the work of Schlesinger were in general unsatisfactory because of the necessity of interpreting the location of the multiple small radicals thus demonstrated and also because of the confusion attendant on interpreting a three-dimensional specimen from a two-dimensional roentgenogram.

Gross[3] in 1921 published a method of visualizing the coronary bed which, although superior to previous methods, still had several disadvantages in that (1) it was a difficult technical procedure requiring complicated apparatus and (2) a period of twenty-four to forty-eight hours had to elapse before the specimen was ready for study.

Schlesinger and his co-workers[2] in 1936 developed a method for visualizing the coronary circulation which was distinctly superior to those previously used. The heart was so dissected that a roentgenogram of the specimen exhibited the coronary arterial circulation in one plane. Technically the method was simple and permitted a study of the circulation in a short time following the autopsy. However, the Schlesinger technique of dissection of the heart so distorts the

From the Department of Medicine, Western Reserve University and the Medical Service, Cleveland City Hospital.

architecture of the valves that they are unsatisfactory for study, and it is here that the pathologist not interested primarily in the minute coronary circulation objects to the trisection of the aortic and pulmonic valves. To meet these objections we have modified the Schlesinger technique of unrolling the heart so as to preserve the valves intact and without distortion.

The initial incision is made through the left cusp of the pulmonic valve and carries down along the entire right border of the interventricular septum to the apex of the heart, opening up the right ventricular cavity (Fig. 1). The second incision is made through the anterior portion of the left coronary cusp of the

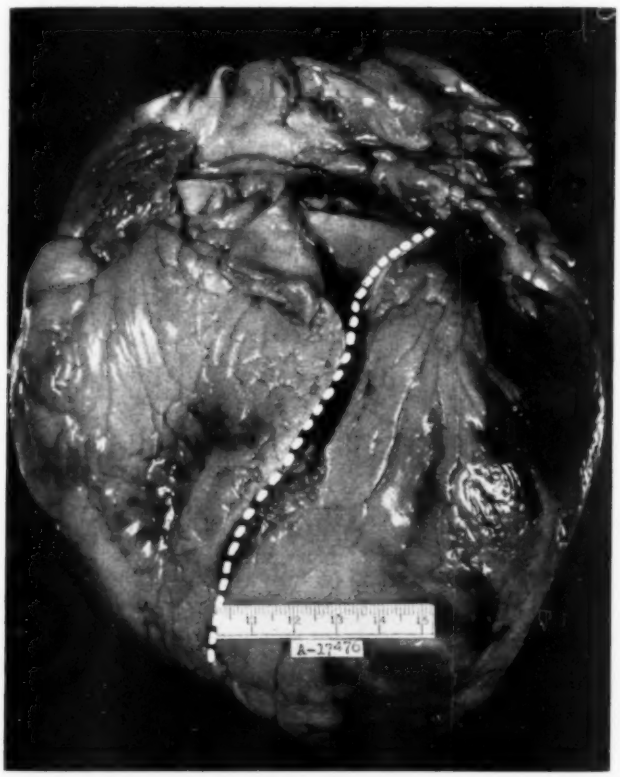


Fig. 1.—Incision made through the left leaflet of the pulmonic valve and extended along the entire right border of the interventricular septum to the cardiac apex.

aortic valve (thus preserving the valve commissure between the right and left coronary cusps) and is extended into the cavity of the left ventricle, care being taken to avoid the main left coronary trunk. This incision is then extended to join the cut surface of the right ventricle and is carried down to the cardiac apex freeing the anterior margin of the septum (Fig. 2). The previously isolated main coronary trunks are now severed from the aorta immediately distal to their ostia with a sharp scalpel and the auricles are widely opened by incisions joining the superior and inferior venae cavae and the pulmonary veins, respectively

A finger can now be readily passed from the left auricle into the left ventricle and dissection scissors guided upward through the lateral margin of the mitral valve orifice and thence between the wall of the aorta and the severed end of the left coronary artery and extending through the auricular musculature. Thus, the entire left side of the specimen is opened. It will be readily unrolled into a single plane after section of two or three chordae tendineae extending to the mitral valve from the posterior papillary muscle. The pulmonary artery segment is now freed from the aortic valve ring by blunt dissection along the planes of cleavage and a similar incision is made on the right side of the interventricular septum (care being taken first to pass an examining finger through the tricuspid

Fig. 2.—Second incision completed through the anterior portion of the left coronary cusp of the aortic valve into the cavity of the left ventricle and then extended to join the cut surface of the right ventricle and down to the cardiac apex.

orifice to facilitate passage of the dissecting scissors upward through the tricuspid valve between the aortic wall and pulmonary artery and avoiding the cut end of the right main coronary trunk), an incision which will enable the right side of the entire specimen to be unrolled for examination (Fig. 3). The final incision consists merely of removal of the interventricular septum in its entirety by dissection through the undefended space and along the posterior border of the septum from base to apex, to connect with the first incision, thus permitting ready removal of the entire septum, which may be placed beneath the main specimen when roentgenograms are made as described by Schlesinger (Fig. 4).

Fig. 3.—Specimen after incisions through the lateral margin of mitral valve and tricuspid valves and extending through the auricular musculature have been completed (lines of incision indicated by dotted lines). The central line represents path of final dissection for removal of the interventricular septum.

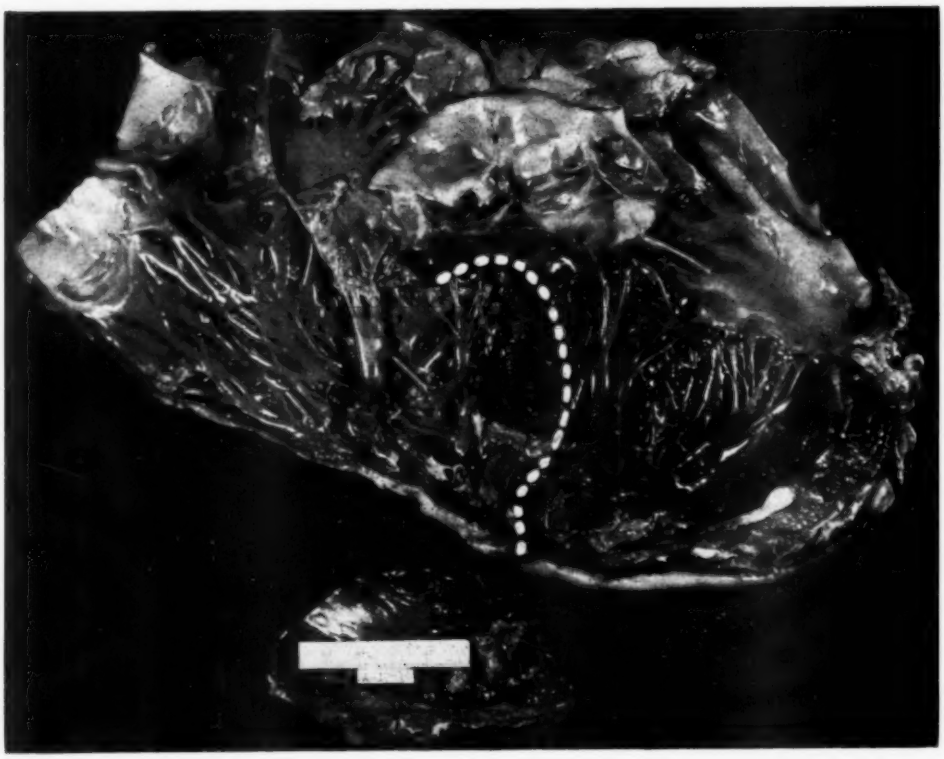


Fig. 4.—Specimen after dissection is completed. The interventricular septum has been removed by dissection through the undefended space and extending along the posterior border of the septum from base of apex.

Fig. 5.—Roentgenogram of normal heart after completion of injection. The anastomotic communications and terminal ramifications of the two main coronary arteries are demonstrated.

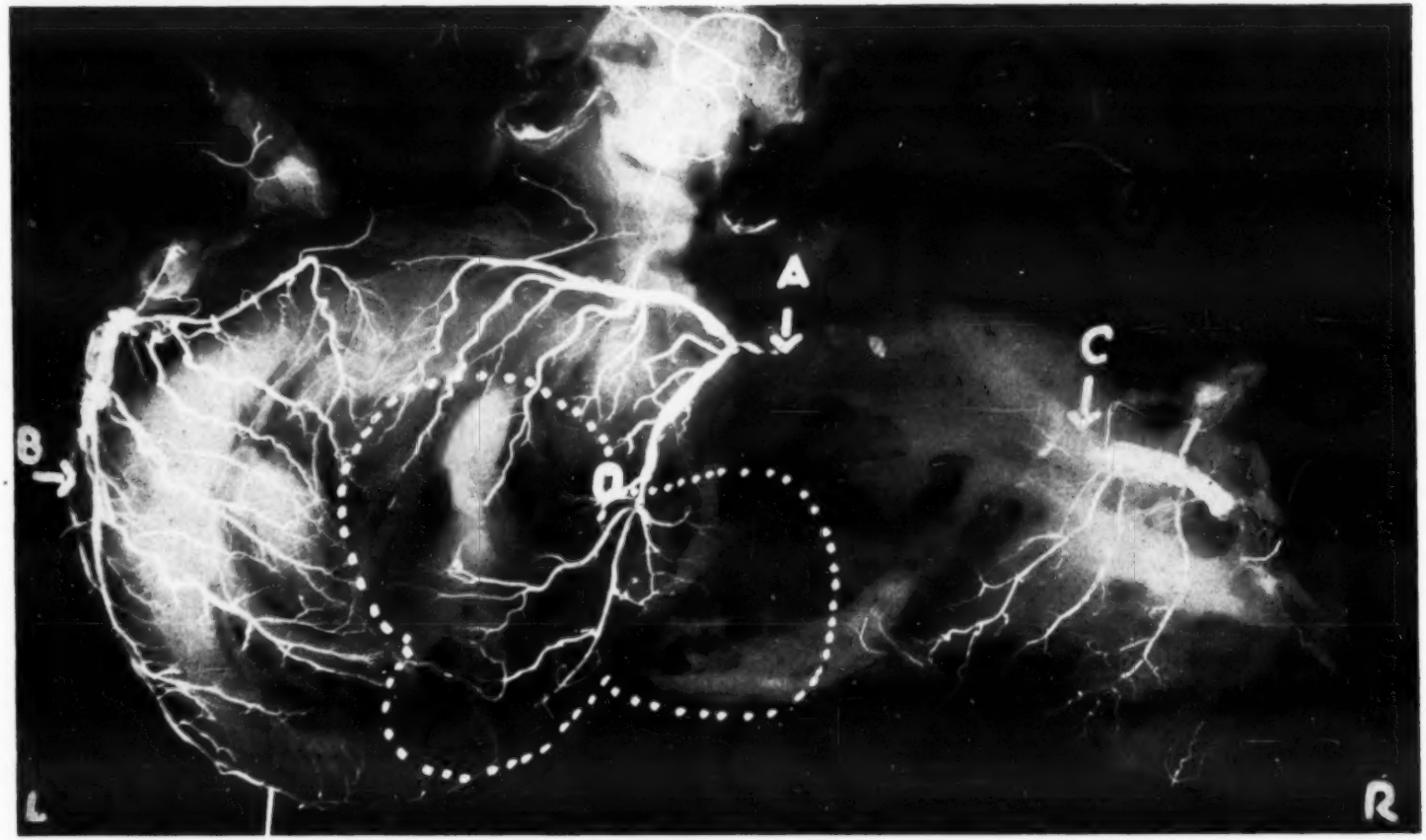


Fig. 6.—Roentgenogram of a specimen showing extensive coronary arteriosclerosis. The main right coronary artery from *C* to *A* was the seat of a fresh thrombus. Both the posterior descending ramus and the terminal right main coronary artery to the left of *A* were filled with red mass injected into the left coronary artery. At *B* was an old occlusion partially recanalized. The area within the dotted line was the seat of fresh infarction.

Salans and Tweed[4] in a preliminary report introduced the use of liquid latex and barium sulfate as the injection mass in an effort to improve the technique described by Schlesinger. This technique, however, necessitated alcohol fixation of the myocardium and subsequent refrigeration which, while time consuming, did not in any way distort the histologic pattern and, in fact, facilitated microscopic examination because the various colors of the injection mass were retained in the histologic preparations.

We have modified the technique of Salans and Tweed as follows: Using their injection apparatus, we have found it unnecessary to suspend the specimen in glacial acetic acid and alcohol as they did; the heart may lie in a flat-bottomed jar during the injection. After the injection it is not necessary to place the specimen in glacial acetic acid and alcohol to harden the injection mass since one may accomplish this by placing the specimen in the standard deep-freeze unit for one and one-half to two hours, after which roentgenograms, as well as sections of the coronary arteries and the myocardium, may be made without any extravasation of the colored injection mass. The injection mass* employed has been that described by Salans and Tweed, except that the particle size of the injection mass has been standardized by screening, ocular micrometer examination, and viscosity determinations, so that the size of the individual particles is standard at 14 micra, a uniformity which permits examination down to and including vessels of this specified caliber but does not extend into the capillary or other small sinusoidal channels.

To facilitate injection we have adopted a method of inserting the glass cannulae into the coronary ostia and fastening them in place as follows: The right and left main coronary trunks are isolated by blunt dissection immediately distal to their respective ostia and a short length of regular upholsterer's thread is passed around the trunk. A glass cannula is then inserted into the coronary ostium. It is secured in place by passing both ends of the previously placed thread through a short length of glass tubing, the ends of which have been especially blunted, and subsequently pulling both sections of thread taut and keeping it so by a small hemostat. This technique of inserting the cannulae is easy and permits their ready removal after the injection is completed.

Roentgenograms† of specimens prepared by our technique are shown in Figs. 5 and 6. Fig. 5 shows a normal coronary bed, while Fig. 6 shows a specimen similarly prepared but one in which the coronary arteries show marked arteriosclerosis and several old occlusions.

---

*A suspension of barium sulfate in an aqueous ammoniated solution of liquid latex is used. Compound No. 60-22724A (red), No. 60-22724B (blue), and No. 60-24899 (white) were obtained from the American Anode Company, Akron, Ohio.

†Two types of film were employed, both screen and nonscreen, in cardboard holders. The technique used with the nonscreen film was 0.3 second, 100 milliamperes, and 44 kilovolts at a 30-inch target-film distance. The technique used with the screen film was 1.0 second, 100 milliamperes, and 40 kilovolts at a 30-inch target-film distance.

SUMMARY

A technique for visualizing the coronary bed of the heart has been described which has certain advantages over previously described methods. It is simple and the entire procedure requires only two hours. The method of dissection preserves the cardiac valves, and the injection mass, which is color fast, does not distort the histologic picture of the myocardium.

The authors gratefully acknowledge the technical assistance of Miss Lucy Krayeris in the development and standardization of the x-ray technique used in this study.

REFERENCES

1. Schlesinger, M. J.: Blood, Heart, and Circulation Symposium, American Association for the Advancement of Science. Publication 13, Washington, D. C., 1940, The Science Press Printing Company, p. 61.
2. Schlesinger, M. J.: Injection Plus Dissection Study of Coronary Artery Occlusions and Anastomoses, AM. HEART J. 15:528, 1938.
3. Gross, L.: The Blood Supply to the Heart, New York, 1921, Paul B. Hoeber, Inc., p. 4-10.
4. Salans, A. H., and Tweed, Phyllis: A Preliminary Study of The Coronary Circulation Post Mortem, AM. HEART J. 33:477, 1947.

NECROSIS IN THE CORONARY ARTERIES OF NEWBORN INFANTS

PETER GRUENWALD, M.D.

BROOKLYN, N. Y.

THE subject of the present report is a necrotic lesion in the coronary arteries of stillborn and newborn infants. In view of its frequent occurrence it appeared desirable to call attention to these findings even though their significance for the function of the heart and for the organism as a whole is not yet understood.

Twenty-one infants listed in Table I showed the lesion which will be described presently. Other pathologic findings in the same infants are also listed, in order that a correlation with the changes in the coronary arteries may be attempted. The considerable frequency of the arterial lesion is evident from Table II. In both tables a prominent place is given to data on the occurrence of those other changes which are commonly interpreted as signs of asphyxia. They include hemorrhages in the epicardium and other parts of the body, aspiration of large amounts of vernix caseosa into the lungs, and general venous congestion. These are the only findings which are nearly constant in the patients with arterial lesions; however, there are many more infants with these signs of asphyxia in which the coronary arteries are not affected. The possible mutual relations of these changes will be discussed. As is often the case in neonatal pathology, no constant and significant data could be obtained from the clinical history.

The majority of the autopsies among which changes in the coronary arteries were encountered were performed at Kings County Hospital. The balance of the material has been obtained through the cooperation of various hospitals in Brooklyn. Tissues were preserved in the usual manner in 10 per cent Formol, Bouin's solution, or Zenker's fixative. Heart sections of one to three paraffin blocks were routinely stained with hematoxylin and eosin. Whenever lesions in the coronary arteries were found or suspected, additional blocks, as well as special stains, were used, including Masson's or Mallory's trichrome stain, Weigert's method for elastic tissue, phosphotungstic acid hematoxylin, and Gömöri's silver impregnation of lattice fibers. Bacterial stains were used in some of the cases and uniformly failed to demonstrate microorganisms in the abnormal areas.

From the Departments of Pathology, Long Island College of Medicine and Kings County Hospital, Brooklyn.

Publication No. 3 of the Brooklyn Survey of Neonatal Pathology. Many hospitals in Brooklyn are contributing pathological material to this survey. The project is supported by a research grant from the Division of Research Grants and Fellowships of the National Institutes of Health, United States Public Health Service.

TABLE I. SUMMARY OF DATA ON TWENTY-ONE INFANTS WITH NECROSIS IN CORONARY ARTERIES

CASE NO.	AGE	BODY LENGTH (CM.)	BODY WEIGHT (GRAMS)	HEMORRHAGES IN			ASPIRATED AMNIOTIC SAC CONTENTS*	OTHER PATHOLOGIC FINDINGS
				EPICARDIUM	PLEURA	OTHER TISSUES		
1	1 day	40	1360	—	—	Kidneys	+++	Dilatation of heart, intraventricular hemorrhage
2	1 day	40½	2000	+	+	Brain, arachnoid	++V	Erythroblastosis, intraventricular hemorrhage, atelectasis
3	10 hours	44	2620	+	+	—	+++V	Subdural hemorrhage
4	31 hours	44½	1470	+	—	—	++M	Esophagitis, conjunctivitis, fatty liver
5	Stillborn	47	2930	+	+	—	++P	—
6	Stillborn	48	2510	+	+	Arachnoid, testes, skin	++	Edema, moderate degeneration of liver
7	Stillborn	48	2620	+	+	—	+++	Conjunctivitis, fatty liver
8	8 hours	49	2470	—	—	Brain	++P	Dilatation of heart, bronchitis, interstitial pneumonia, esophagitis, perisplenitis
9	3 days	49½	2400	+	+	—	+P	Intraventricular, subdural hemorrhage; fatty liver
10	Stillborn	49	3180	+	+	—	++	—
11	2 days	50	3030	+	+	—	++P	Enlargement of heart and liver, intraventricular hemorrhage
12	Stillborn	51	3160	+	+	Thymus, testes	+	Moderate hydroureter, moderate degeneration of liver
13	8 hours	51	3190	+	+	—	+++	Pleuritis, interstitial emphysema of lungs
14	16 hours	51	4320	+	+	Brain	+++P	Dilatation of heart, horseshoe kidney
15	11 hours	51½	2750	+	+	—	+++M	Dilatation of heart, pleuritis, erosions in stomach
16	45 min.	53	3120	+	—	Testes	++	Interstitial emphysema of lungs
17	36 hours	53	3580	+	—	Arachnoid	+++P	Dilatation of heart, congestion and edema of brain, esophagitis, bilateral club foot
18	21 hours	54	4010	—	+	—	+++P	Jaundice, edema of brain, esophagitis, pancreatitis
19	Stillborn	54	4570	+	—	—	+++M	Enlargement of heart, liver, spleen, adrenals; rupture of liver with hemoperitoneum; pancreatitis; edema of brain
20	1 day	55	3300	+	—	—	++M	Dilatation of heart, fatty liver, esophagitis, intraventricular hemorrhage
21	Stillborn	56	3300	+	+	—	++P	Pleural effusion, cephalhematoma, subdural hemorrhage

*M, aspiration of meconium; P, pneumonia; V, vernix membranes.

TABLE II. CORRELATION OF NECROSIS IN CORONARY ARTERIES WITH HEMORRHAGES IN THE EPICARDIUM, AND BODY LENGTH IN INFANTS UP TO THREE DAYS OF AGE, INCLUDING NONMACERATED STILLBORN INFANTS

	ALL INFANTS EXAMINED		CASES WITH NECROSIS IN CORONARY ARTERIES		
	NUMBER OF CASES	AVERAGE BODY LENGTH	NUMBER	PER CENT	AVERAGE BODY LENGTH
Hemorrhages in epicardium	98	45.3	18	18.4	49.9
No hemorrhages in epicardium	123	40.2	3	2.4	47.7
Total	221		21	9.5	

The essential features of the abnormality are best described by referring to typical lesions, as illustrated in Figures 1 to 8. The most conspicuous form of the lesion is exemplified by Case 13 (Fig. 1). At the border of the media and the adventitia of many arteries there are masses of eosinophilic material enclosing cavities filled with debris and an occasional erythrocyte. In some instances these areas are small, and in others they surround most or all of the vessel. The abnormal material extends toward the lumen of the artery to a varying extent, replacing part of the media. In the present patient most of the lesions do not penetrate the entire thickness of the media, and the intima is intact everywhere. The affected arteries are dilated, and the internal elastic membrane shows little or none of the scalloping which would indicate a contraction of the media. The tissue surrounding these arteries shows greatly dilated veins and capillaries, as well as extravasation of blood from the vessels, as it is commonly seen in the epicardium of asphyxiated newborn infants. There is moderate increase in the number of various white blood cells distributed in the tissue spaces of the epicardium. The lungs in this infant showed interstitial emphysema, with collections of air in the septa and under the pleura. Some of these spaces were partly filled with turbid fluid, and about 10 c.c. of similar fluid was contained in each pleural cavity. Bacterial cultures and stains were negative.

Case 10 shows the typical hemorrhages in pleura and epicardium which are often associated with asphyxia (Fig. 2). In the arteries in the epicardium there are again foci of eosinophilic material, in this patient replacing the entire media (Fig. 3); they do not contain the large vacuoles seen in Case 13. There are a few distorted nuclei in these areas. The intima is intact. Dilatation of all vessels and extravasation of blood are present as in the preceding patient, but there is no appreciable infiltration with white blood cells.

A greater variety of changes is found in the coronary arteries of Case 16, both in the epicardium and in the myocardium. In addition to areas resembling that shown in Fig. 3, there are others in which the media is transformed into a group of spaces filled with finely granular material (Fig. 4) which is more uniform in appearance than the debris shown in Fig. 1. In large areas the media is entirely destroyed, and extravasated blood is seen surrounding the intact intima (Fig. 4). The same patient shows a peculiarity which is not typically associated with the

lesion under consideration, namely, thrombosis in the lumen of arteries (Fig. 5). Only one other instance of thrombosis has been found (Case 8). In both these patients the thrombi were attached to damaged portions of the vessel wall. They are small and have never been seen completely occluding the lumen.

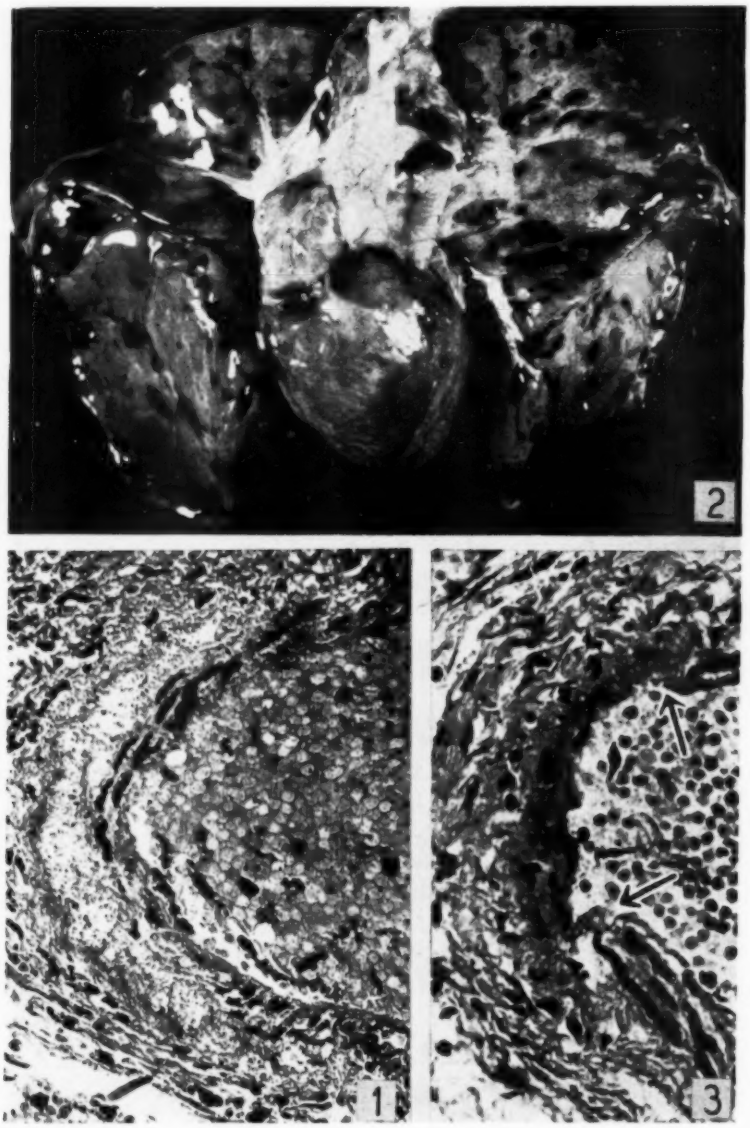


Fig. 1.—An artery in the epicardium of Case 13. The inner portion of the media is preserved and the nuclei of its muscle fibers are seen. The outer portion is replaced by an eosinophilic mass with cavities filled with granular debris. (×350)

Fig. 2.—Thoracic viscera of Case 10, showing numerous areas of hemorrhage in epicardium and pleura.

Fig. 3.—A coronary artery of Case 10 (see also Fig. 2), showing, between the arrows, an area in which the media is replaced by homogeneous, eosinophilic material. (×500)

Another example of transformation of the media into a necrotic mass with cavities filled with granular debris is Case 21 (Fig. 6). In this patient there are also arteries in which the media has disappeared, and a moderate aneurysmal dilatation has occurred. This dilatation seldom exceeds in width the space vacated by the disappearance of the media, and an intact internal elastic layer can be demonstrated throughout the lesion (Fig. 7). In other instances, such as that shown in Fig. 8 (Case 3), the media disappears without leaving a trace, and without the development of bulging of the weakened vessel walls.

The lesions in all other cases listed in Table I conform to the descriptions just given. The occurrence of the various forms of necrosis in each patient will not be described in detail.

Fig. 4.—An artery in the myocardium of Case 16. The media is preserved only in the lowermost portion of the figure. The remainder of the media is either destroyed and replaced by hemorrhage, or transformed into cavities filled with finely granular material (at arrow). (×350)

Fig. 5.—An artery in the epicardium of the same patient shows a small thrombus in the lumen, attached to a portion of the wall in which the intima cannot be seen, and the media is replaced by eosinophilic material. (×250)

Search of the literature has revealed only one report possibly related to the changes under consideration.[1] This was the case of a 3-day-old infant in which the intima and adjacent portion of the media of the coronary arteries was intact, whereas the outer portion of the wall stained poorly and had an "almost hyaline-like"[1] appearance. The published description and figures do not permit a decision as to whether or not this is an instance of the same pathological condition as that described here. One wonders why these conspicuous lesions have not received more attention in the past. This is probably not due to oversight on the

part of previous investigators, but rather to the assumption that the changes in question are artifacts. This possibility must be taken into account. The present material includes tissue preserved in various hospitals with different

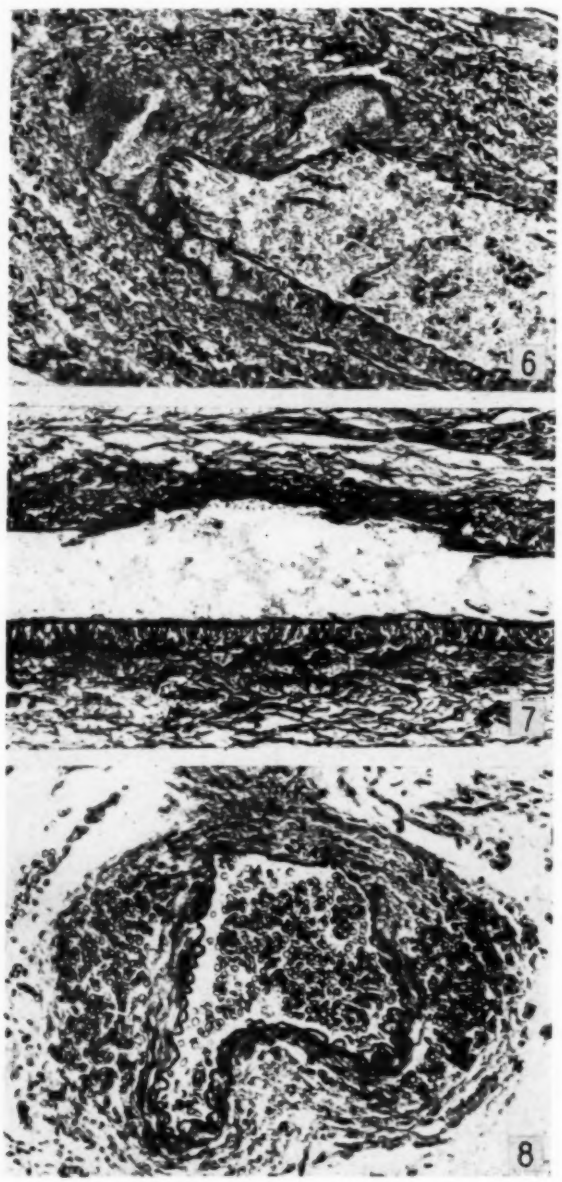


Fig. 6.—A coronary artery of Case 20, with partial destruction of the media and formation of cavities filled with granular material. (×250)

Fig. 7.—An artery in the myocardium of the same patient shows an area of disappearance of the media, with bulging of the intact intima. (×250)

Fig. 8.—A coronary artery of Case 3. In the upper portion of the figure no media is seen, and the internal elastic membrane borders directly on the adventitia. Other arteries in this patient showed changes similar to those illustrated in the preceding figures. (×250)

fixatives. In the majority of the cases the preservation of the tissues is generally good, and changes similar to those in the heart were found only in the liver, as will be mentioned subsequently. All these factors indicate that one is not dealing with artifacts. Relying on these facts, as well as on the observation of various stages of the lesion and their demonstration with a variety of staining methods, the conclusion that the changes occurred during life has been reached.

The following common features are present in the great majority of all foci of necrosis. The outer portion of the media is affected, and tissue damage may extend inward to a varying depth. The adventitia is the seat of edema and hemorrhage, and, in a few instances, also of a moderate leucocytic infiltration. The intima is usually intact, which accounts for the fact that thrombosis in the lumen is not the rule. The above-mentioned change in the adventitia is not limited to those areas in which the media is visibly damaged. It is widely distributed along the vessels of the heart in these infants, as well as in others showing congestion and foci of hemorrhage, as these conditions are commonly believed to be associated with anoxia. This association will be discussed. At this point it should be emphasized that necrosis of the media occurs in some of those areas in which edema and hemorrhage have affected the adventitia. This fact, together with the observation that the lesion appears to progress from the adventitia toward the intima, suggests that perhaps the nutrition of the vessel wall, derived from the adventitia, is defective in the areas of necrosis. A thin, inner layer of the vessel wall, comprising the intima and in some cases the adjacent part of the media, may be assumed to be preserved because it draws its supplies from the lumen of the artery.

It is difficult to judge the extent to which necrosis in the media of arteries, as described here, affects the function of these vessels. Extreme dilatation of the artery is not limited to the segments with visible damage to the media, but occurs throughout the heart of an asphyxiated newborn infant, regardless of the occurrence of necrosis. Electrocardiographic evidence suggests myocardial damage in asphyxiated newborn infants,[2] but there is no reason to believe that this depends on the changes described here. Thrombosis in arteries with necrosis is rare and never complete, and rupture of an artery has not been seen. It is possible, therefore, that arteries with necrosis do not differ functionally from others in the same organ. Whether recovery from anoxia is influenced by necrosis in the media is not known.

It will be noted that no late stages were observed in older infants, and this indicates either that all infants with these lesions die, or that the destroyed tissue regenerates rapidly. The former alternative could mean that the lesion in question is fatal, or that it is a terminal event. The possibility of rapid and complete regeneration must be seriously considered, since the regenerative power of the tissues may well be greater in the newborn than in the adult, who serves as the standard in human pathology. At this time, no decision can be made as to which of the above-mentioned possibilities is correct.

Search for the cause of necrosis in the wall of coronary arteries must take into account the following facts. All instances were observed in infants who were stillborn, or who died shortly after birth (Table I). This points to a causal

connection with some agent active about the time of birth. The only significant and nearly constant correlation with other pathological changes is that with hemorrhages in thoracic viscera (including the epicardium itself) and with aspiration into the lungs of large amounts of amniotic sac contents, including vernix. Both of these findings are generally believed to indicate paranatal anoxia. In order to obtain further information regarding this point, a survey was made of all newborn infants who showed, at necropsy, hemorrhages of the epicardium and other parts of the body (Table II). This group of infants was studied during the same period in which the instances of necrosis were collected.

It is apparent from Table II that necrosis in the coronary arteries occurs more than seven times as frequently in infants with the typical asphyxial hemorrhages in the epicardium as in those without such hemorrhages. It might be added that in the majority of the infants with necrosis and hemorrhages the latter were present in other organs as well. Even in the three infants in whom hemorrhages were not found in the epicardium, they were present in other organs (Table I). It can further be seen (Table II) that the average body size of infants with epicardial hemorrhages (45.3 cm.) is larger than that of infants without them (40.2 cm.). Infants with necrosis in the coronary arteries are in turn longer (49.4 cm.) than the average of the unselected group with hemorrhages. This may be because a larger infant is likely to suffer more anoxia at birth than a smaller one. Several older infants have been examined in whom numerous hemorrhages in the pleura and epicardium existed, usually associated with extensive pneumonia. None of these infants showed any abnormalities in the coronary arteries.

All these considerations point to anoxia at birth as the cause of the necrotic lesions. It is known that the newborn infant tolerates more anoxia than does the adult.[3,4] While this is doubtless an advantage in many instances, it may in other cases permit the development of changes which could not arise in older individuals because they could not survive sufficiently long.

The only report found in the literature which links necrosis in the media of arteries with anoxia is that of Gürich[5], who found necrosis in the media of cerebral arteries in fatal poisoning with illuminating gas. Kernohan and Woltman[6] described focal necrosis of vertebral and cerebellar arteries with rupture, occurring after abdominal operations. It appears to this writer that the only common denominator of these cases of anoxia and postoperative state could be shock.

Dilatation of the heart was sufficiently severe to be mentioned in six cases at the time of autopsy, before the change in the arteries was known. This may be due to anoxia of the myocardium, as well as embarrassed pulmonary circulation due to massive aspiration of the contents of the amniotic sac and, in some cases, to pneumonia.

The severity of hemorrhages in the epicardium and in other parts of the body is not proportionate to the degree of damage to the arteries. In several patients with very extensive hemorrhages in the thoracic organs, many sections of the heart were searched in vain for necrosis of the arteries. Other factors are apparently involved, and one of these may be the length of survival after the height of anoxia. One may expect that a longer time is required for necrosis in

the media of arteries to become apparent than for extravasation of blood from capillaries.

After the examination of the lesions in the coronary arteries was nearly completed, similar changes were found in the arteries of the liver of four newborn infants with normal coronary arteries. Three of them showed marked signs of asphyxia. Renewed examination of the organs of the infants with changes in the coronary arteries revealed similar changes in the liver of two of them (Cases 16 and 18). The evaluation of this observation cannot be attempted until more information is available. So far, no other organ has been found to be affected.

SUMMARY

Necrosis in the media of coronary arteries has been found in twenty-one newborn or stillborn infants or in 9.5 per cent of the autopsies performed on infants up to three days of age. These infants showed various degrees of the common signs of asphyxia, including focal hemorrhages in thoracic and other organs and aspiration of unusually large amounts of vernix caseosa.

The outer part of the media is consistently affected, whereas the inner part is spared in some instances. The intima is intact almost without exception. Small thrombi were found in two cases. Rupture of an artery has not been observed.

The adventitia is the seat of edema and hemorrhage, as it is also found to be in infants with signs of asphyxia but without necrosis. There are indications that necrosis in the media is secondary to a change in the surrounding tissue, and that it may appear only after the latter has reached a certain limit of intensity and duration.

The significance of necrosis in the media of coronary arteries of the newborn infant is not known. As a rule, the vessels in the heart of an asphyxiated infant are greatly dilated, regardless of the presence of necrosis. No healing stages of the lesion have been found. Healing may be complete, or the lesion may be fatal, or terminal.

REFERENCES

1. Kissane, H. W., and Fidler, R. S.: Congenital Medial Sclerosis of the Coronary Artery, Am. Heart J. **7**:133, 1931.
2. Hori, H., Imai, M., and Sato, M.: On the Electrocardiogram of the Newborn. II. On the Electrocardiogram of the Asphyxiated Newborn, Jap. J. Obst. & Gynec. **18**:333, 1935.
3. Himwich, H. E., Alexander, F. A. D., and Fazekas, J. F.: Tolerance of the Newborn to Hypoxia and Anoxia, Am. J. Physiol. **133**:327, 1941.
4. Wilson, J. L., Reardorn, H. S., Murayama, M., Graham, B., Tsao, M. U., and Baumann, M. L.: Anaerobic Metabolism in the Newborn Infant. I. On the Resistance of the Fetus and Newborn to Oxygen Lack, Pediatrics **1**:591, 1948.
5. Gürich: Herzmuskelveränderungen bei Leuchtgasvergiftung, Münch. Med. Wchnschr. **72**:2194, 1925.
6. Kernohan, J. W., and Woltman, H. W.: Postoperative, Focal, Nonseptic Necrosis of Vertebral and Cerebellar Arteries With Rupture and Subarachnoid Hemorrhage, J. A. M. A. **122**:1173, 1943.

Clinical Reports

POLYARTERITIS NODOSA OF THE CORONARY ARTERIES

Report of a Case in an Infant With Rupture of an Aneurysm and Intrapericardial Hemorrhage

William Sinclair, Jr., M.D., Cleveland, Ohio, and
Emilia Nitsch, M.D., Lakewood, Ohio

POLYARTERITIS nodosa is a rare disease in infants and children.[1,2,3] The disease may be confined to the coronary arteries, or these may be affected when the arteritis is more widespread. Aneurysms may develop in the coronary arteries, and rupture leads to hemopericardium. Thrombosis may result in myocardial infarction. There have been few isolated case reports regarding such occurrences.[4,5,6]

It is the purpose of this paper to record such a case, to review similar previously reported cases, and to comment briefly on current concepts of the etiology of this disease.

CASE REPORT

A white female infant 9 months of age was admitted to Babies and Childrens Hospital on March 16, 1948 by one of us (E. N.). She had been well except for slight stridor until five days before admission, when a tender, soft mass was noted at the angle of the left jaw. The following day the temperature rose to 40°C. and the patient became listless. A diagnosis of pharyngitis and adenitis was made and sulfadiazine was given, but most of the medication was vomited. The fever persisted and the mass enlarged. Penicillin in beeswax and oil was administered intramuscularly. On the day before admission the mass at the angle of the jaw was incised, and drainage of a small amount of mucus and puslike fluid took place. The infant was hospitalized because of persistent fever, irritability, restlessness, and continuous drainage from the incision. There was no history of any allergy or of previous sulfonamide medication.

Physical examination revealed a well-developed and well-nourished, pale infant who was acutely and seriously ill. The temperature was 40°C.; the pulse rate, 200; and the respiratory rate, 70. The papillae of the tongue were large. There was slight stiffness of the neck. A firm mass measuring 1.5 cm. in diameter was palpable beneath the incision in the neck. Small amounts of bloody fluid drained from the opening. The physical examination otherwise was not remarkable.

Laboratory studies included the following: Urinalyses revealed 1 plus albumin and 18 to 20 white blood cells per high-power field. Two urine cultures were sterile. The red blood cell

From the Institute of Pathology, Western Reserve University, and the University Hospitals of Cleveland.

count was 2.4 million; the hemoglobin was 42 per cent; the white blood cell count 14,500, with a differential count of 65 segmented neutrophiles, 17 unsegmented neutrophiles, 12 lymphocytes, and 6 monocytes. The platelet count was 248,880. The bleeding and clotting times were normal. A Kline test was negative. The blood pH, serum proteins, calcium, phosphorus, potassium, and sodium levels were normal. Examination of the spinal fluid yielded 31 mononuclear cells and 1 neutrophile. There were 48.5 mg. of protein per 100 c.c., and 87.5 mg. of sugar per 100 cubic centimeters. A 1:1000 tuberculin test was negative.

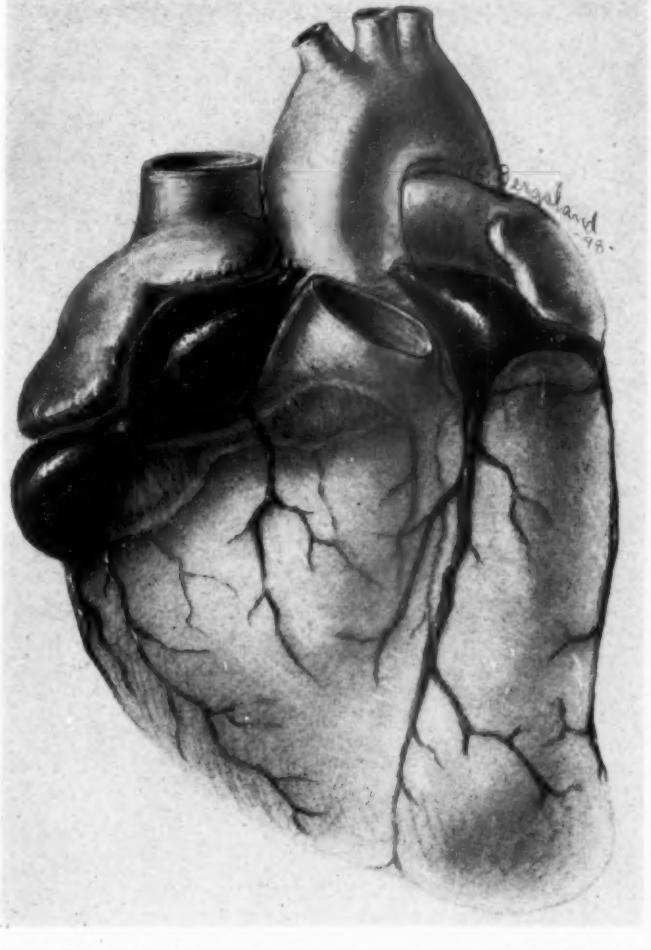


Fig. 1.—Diagram illustrating distribution of aneurysms. The lightly shaded artery is on the posterior wall of the right ventricle.

On the second hospital day the infant developed a faint macular rash over the abdomen. On the following day the rash had spread to the arms and legs and was more pronounced. The conjunctiva became inflamed and the periorbital tissues became swollen. The mucous membranes of the mouth and vulva were markedly hyperemic. The temperature ranged between 39° and 40° centigrade. The white blood cell count rose to 23,000. The rash, conjunctivitis, stomatitis, and vaginitis gradually disappeared after five days, and the swelling in the neck regressed almost entirely. However, the temperature remained elevated and the infant appeared seriously ill. Treatment consisted of penicillin, sulfadiazine, one whole blood tranfusion, pheno-

barbital, frequent infusions of glucose in saline, and the application of boric acid solution and penicillin topically to the conjunctiva. Blood cultures and agglutination studies for typhoid and paratyphoid A and B were negative. Cold agglutinin studies were not obtained. X-ray examinations of the chest showed accentuated bronchovascular markings in both lungs and increased convexity of the left cardiac border. An electrocardiogram was not obtained.

On the twelfth hospital day the temperature gradually dropped, and remained between 38° and 38.5° centigrade. The white blood count fell to 14,000, with a normal differential. Sulfadiazine was discontinued on the eighteenth day. The child was considered well enough to be discharged, but because of persistent stridor, laryngoscopy was performed on the twenty-second hospital day. The larynx appeared normal. The laryngoscope was withdrawn during what appeared to be laryngeal spasm and the child failed to breathe. An airway was immediately inserted and artificial respiration started, but the infant had died.

Fig. 2.—Photograph of heart showing cross section of second aneurysm of right coronary artery.

Autopsy (10074).—The heart weighed 53 grams (expected weight, 37 grams). The pericardial sac was filled with 50 c.c. of clotted blood, which encased the heart. The parietal pericardium was normal. The epicardium about the coronary arteries was opaque, thickened slightly, rough, and partially covered with fibrin; elsewhere it was normal. The myocardium was everywhere firm, and was reddish-brown and of normal thickness. All valves had a normal configuration and circumference. The foramen ovale and ductus arteriosus were closed.

The coronary ostia were normally located and measured 1.0 mm. in diameter. The right coronary artery was greatly deformed by three fusiform aneurysms. The proximal one arose 1.0 mm. distal to the ostium and extended 20 millimeters. The dilated lumen attained a maximum diameter of 8.0 millimeters. The walls were firm, opaque, and gray, and varied from 1.0 to 4.0 mm. in thickness, except in the midportion on the anterior surface, where the wall was discolored reddish-brown and measured less than 1.0 mm. in thickness. A definite perforation could not be seen in the gross specimen at this site, but subsequent microscopic studies revealed a perfora-

tion through the wall in this locus. Attached to the wall in this region was a small amount of adherent, friable, reddish-brown and gray material. At the distal segment the lumen abruptly narrowed to a diameter of 1.0 mm. for a distance of 2.0 millimeters. Distal to this constriction the artery again became dilated and formed a second fusiform aneurysm measuring 15 by 9 millimeters. The wall was similar to that previously described, but was intact. As the artery coursed along the posterior and basal portions of the right ventricle, the lumen gradually dilated, reaching a maximum internal diameter of 4.0 mm., and then gradually returned to normal. This involved a portion measuring 12 mm. in length. The secondary branches of the artery were not remarkable.

The left coronary artery presented a single, similar aneurysm which arose 1.0 mm. distal to the ostium and measured 15 mm. in length and 7.0 mm. in diameter. The proximal portion of the circumflex and left anterior descending arteries was involved for a short distance. The coronary veins were normal. There were no significant gross lesions in other organs.

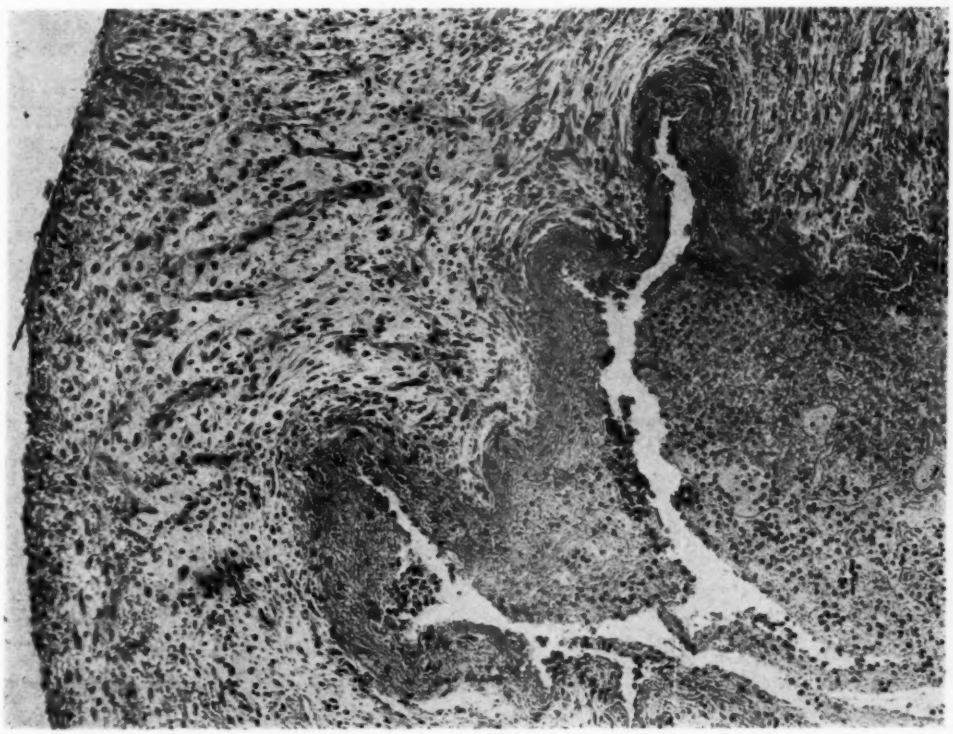


Fig. 3.—Photomicrograph (× 102) of wall of first aneurysm of right coronary artery. Note mural thrombus, variation in thickness of wall, loss of normal pattern, and necrotizing and exudative character of inflammation.

Microscopic studies of the coronary arteries demonstrated involvement of all layers and of the entire circumference of the wall. The intima was replaced by edematous organizing granulation tissue consisting of fibroblasts, mononuclear macrophages, numerous thin-walled vascular channels, a rich infiltration of lymphocytes, eosinophils, and neutrophils, and a few erythrocytes. Deposited upon the surface in many regions was a thin layer of fibrin and granular eosinophilic material enmeshing neutrophils, and into this layer capillaries extended. The internal elastic membrane was not recognizable. The media was almost completely replaced by organizing granulation tissue similar to that already described, which, in addition, contained many more extravasated erythrocytes. In most foci muscle was lacking, while in other regions necrotic muscle was present. The adventitia and adjacent subepicardial fat were likewise involved.

The destruction of the wall was so complete that in many places distinction of the various layers was impossible. In no instance was bacterial colonization evident. The proximal aneurysm of the right artery was perforated. The neighboring intima was the seat of an organizing mural thrombus. The adjacent myocardium was slightly infiltrated with neutrophils and a few lymphocytes, and the epicardium was notable because of focal organizing acute epicarditis. These changes were confined to the main coronary arteries. All other arteries were normal.

Significant anatomic diagnoses were acute and organizing necrotizing exudative arteritis of the coronary arteries morphologically identical with polyarteritis nodosa, multiple aneurysms of the coronary arteries with rupture of the proximal aneurysm of the right coronary artery, organizing mural thrombus of the right coronary artery, hemopericardium, slight focal acute and chronic exudative myocarditis, focal organizing acute epicarditis, slight focal acute interstitial pneumonitis, slight acute bronchitis, and eosinophilic infiltration of the pulp of the spleen.

DISCUSSION

This case is unusual, and worthy of note for several reasons. First, it is the sixth case of polyarteritis nodosa reported in infants under 1 year of age.[5,7] Second, the disease was confined to the coronary arteries. Third, the polyarteritis nodosa resulted in multiple aneurysms of the coronary arteries, one of which ruptured into the pericardial sac. Fourth, the clinical features of fever, conjunctivitis, stomatitis, vaginitis, an erythema multiforme type of skin rash, and lack of response to sulfonamides and penicillin are suggestive of viral disease and resemble in many ways a mild form of Stevens-Johnson syndrome.[8] Finland, Jolliffe, and Parker[9] described four cases of Stevens-Johnson syndrome in which evidence of infection with a psittacosis-like virus was obtained in three patients. None of these patients, however, had polyarteritis nodosa.

The inflammatory character of the reaction clearly distinguishes these lesions from congenital aneurysm of the coronary arteries as described and reviewed by Harris,[10] who attributed this anomaly to deficiency in elastic tissue.

Pickard, Owen, and Dammin[4] have reported a case similar in many respects to ours. Their patient was a 15-month-old female infant who three months before death had been hospitalized for rash (erythema multiforme), fever, conjunctivitis, and pharyngitis. Three weeks before death the infant developed cardiac failure and died shortly after her second admission to a hospital. Autopsy disclosed healing and healed polyarteritis nodosa of the coronary arteries, multiple aneurysms of the coronary arteries, coronary thrombosis, and myocardial infarction. Scott and Rotondo[5] reported the finding of aneurysms of the coronary arteries due to polyarteritis nodosa in two white female children, aged 5 years and 9 months, respectively. Rupture with intrapericardial hemorrhage occurred in one and was considered "imminent" in the other. In the older patient, only the coronary arteries were involved, whereas the coronary, renal, hepatic, and uterine arteries were involved in the infant. The clinical features were similar to those of our patient.

Spector[6] recorded the occurrence of scarlet fever, periarteritis nodosa limited to the coronary arteries, and aneurysms of the coronary arteries with spontaneous rupture and hemopericardium in a 5-year-old white girl. Vance and Graham's[11] patient was a 21-year-old Negro man who had widespread periarteritis nodosa complicated by rupture of an aneurysm of the left coronary artery, with fatal intrapericardial hemorrhage.

Since Von Rokitansky's paper[12] in 1852, and Kussmaul and Maier's[13] classic presentation in 1866, polyarteritis nodosa has been the subject of extensive study, discussion, and speculation. The protean clinical manifestations have long been recognized. In recent years attention has been focused chiefly on etiology and pathogenesis, with major emphasis placed on the role of hypersensitivity originally suggested by Gruber[14] in 1925. In 1943, Rich and Gregory[15] produced necrotizing vascular lesions in rabbits made hypersensitive to sterile horse serum. These studies were prompted by the observation of polyarteritis nodosa in patients with serum sickness and in those treated by sulfonamide therapy.[16] Their work has been confirmed by Hawn and Janeway,[17] McKeown,[18] and recently by Orbison[19] at this institute. On the other hand, Fox and Jones[20] and Smith and Zeek[21] were unable to produce polyarteritis nodosa even though their rabbits were made hypersensitive. The last-named investigators placed importance upon the role of sharply rising hypertension as a major factor in pathogenesis.

In 1933, Landsteiner and Van der Scheer[22] produced specific hypersensitivity to nonantigenic azo dyes by combining these substances with protein. These studies and others cited by them have provided a framework for the recent concept of polyarteritis nodosa as a manifestation of hypersensitivity to sulfonamides,[15,23,24] iodine,[25] thiouracil,[26] phenobarbital,[21] and possibly other chemicals which ordinarily are nonantigenic. Karsner[27] distinguished polyarteritis nodosa as a primary arteritis distinct from secondary arteritis of bacterial origin, and laid significance upon the presence of eosinophils in the involved tissues.

In the 1920's virus infection was considered by some investigators[28,29,30] to be a likely causative agent, but no virus has been isolated or established as a factor beyond doubt. We have been unable to find any reports on virus infection as a cause in a review of the literature of the past twenty years, and conclude that this concept has been overshadowed by the prevailing hypothesis of hyperergy. Although the clinical features of our patient suggested a viral origin, we do not propose to imply that this was the case, but merely desire to call attention to the older idea of virus infection as an excitor of this disease. With the newer techniques and the increasing opportunity for the study of viruses, it is anticipated that further investigation of this problem will be forthcoming. Likewise, we believe that in this instance it is impossible to state with any assurance the role played by sulfadiazine and other medication in the production of polyarteritis nodosa.

SUMMARY

A case of polyarteritis nodosa in a white female infant 9 months old is reported. The process was confined to the coronary arteries and was complicated by rupture of an aneurysm with subsequent intrapericardial hemorrhage.

Five similar previously reported cases are summarized. The observations of various investigators pertaining to the role of hypersensitivity to foreign protein, and to the role of sulfonamides and other chemicals which ordinarily are nonantigenic are discussed. The nonbacterial nature of primary arteritis is mentioned. Attention is called to the older hypothesis of virus as an etiological agent. It is not possible in this instance to state what the specific exciting factor was in the production of polyarteritis nodosa.

REFERENCES

1. Keith, H. M., and Baggenstoss, A. H.: Primary Arteritis (Periarteritis Nodosa) Among Children, J. Pediat. **18**:494, 1941.
2. Rothstein, J., and Welt, S.: Periarteritis Nodosa in Infancy and in Childhood, Am. J. Dis. Child. **45**:1277, 1933.
3. Stryker, W. A.: Coronary Occlusive Disease in Infants and Children, Am. J. Dis. Child. **71**:280, 1946.
4. Pickard, C. M., Owen, J. G., and Dammin, G. J.: Aneurysms of the Coronary Arteries Due to Polyarteritis Nodosa Occurring in an Infant: Report of a Case With Coronary Artery Thrombosis and Myocardial Infarction, J. Lab. & Clin. Med. **32**:1513, 1947.
5. Scott, E. P., and Rotondo, C. C.: Periarteritis Nodosa: Report of Two Cases, One Complicated by Intrapericardial Hemorrhage, J. Pediat. **25**:306, 1944.
6. Spector. S.: Scarlet Fever, Periarteritis Nodosa, Aneurysm of Coronary Artery With Spontaneous Rupture, Hemopericardium, Arch. Pediat. **56**:319, 1939.
7. Wilmer, H. A.: Two Cases of Periarteritis Nodosa Occurring in the First Month of Life, Bull. Johns Hopkins Hosp. **77**:275, 1945.
8. Stevens, A. M., and Johnson, F. C.: A New Eruptive Fever Associated With Stomatitis and Ophthalmia, Am. J. Dis. Child. **24**:526, 1922.
9. Finland, M., Jolliffe, L. S., and Parker, F.: Pneumonia and Erythema Multiforme Exudativum: Report of Four Cases and Three Autopsies, Am. J. Med. **4**:473, 1948.
10. Harris, P. N.: Aneurysmal Dilatation of the Cardiac Coronary Arteries, Am. J. Path. **13**:89, 1937.
11. Vance, B. N., and Graham, J. E.: Periarteritis Nodosa Complicated by Fatal Intrapericardial Hemorrhage, Arch. Path. **12**:521, 1931.
12. Von Rokitansky, C. F.: Denkschr. d. k. Akad. d. Wissensch. Wein. 4,[r]1852. (Cited by various authors.)
13. Kussmaul, A., and Maier, R.: Ueber ein bisher nicht beschriebene eigenthümliche Arterienerkrankung (Periarteritis nodosa), Deutsches Arch. f. klin. Med. **1**:484, 1866.
14. Gruber, G. B.: Zur Frage der Periarteritis nodosa mit besonderer Berücksichtigung der Gallenblassen—und Nieren beteiligung, Virchows Arch. f. path. Anat. **258**:441, 1925.
15. Rich, A. R., and Gregory, J. E.: The Experimental Demonstration That Periarteritis Nodosa Is a Manifestation of Hypersensitivity, Bull. Johns Hopkins Hosp. **72**:65, 1943.
16. Rich, A. F.: The Role of Hypersensitivity in Periarteritis Nodosa, As Indicated by Seven Cases Developing During Serum Sickness and Sulfonamide Therapy, Bull. Johns Hopkins Hosp. **71**:123, 1942.
17. Hawn, C. U., and Janeway, C. A.: Histological and Serological Sequences in Experimental Hypersensitivity, J. Exper. Med. **85**:571, 1947.
18. McKeown, E. F.: Experimental Serum Carditis and Its Relationship to Rheumatic Fever, J. Path. & Bact. **59**:547, 1947.
19. Orbison, J. L.: Personal communication, June, 1948.
20. Fox, R. A., and Jones, L. R.: Vascular Pathology in Rabbits Following Administration of a Foreign Protein, Proc. Soc. Exper. Biol. & Med. **55**:294, 1944.
21. Smith, C. C., and Zeek, P. M.: Studies on Periarteritis Nodosa. II. The Role of Various Factors in the Etiology of Periarteritis Nodosa in Experimental Animals, Am. J. Path. **23**:147, 1947.
22. Landsteiner, K., and van der Scheer, J.: Anaphylactic Shock by Azodyes, J. Exper. Med. **57**:633, 1933.
23. Lichtenstein, L., and Fox, L. J.: Necrotizing Arterial Lesions Resembling Those of Periarteritis Nodosa and Focal Visceral Necrosis Following Administration of Sulfathizaole, Am. J. Path. **22**:665, 1946.
24. Goodman, M. J.: Periarteritis Nodosa With Recovery; Report of an Unusual Case Apparently Due to Sensitivity to Sulfadiazine, Ann. Int. Med. **28**:181, 1948.
25. Rich, A. R.: Hypersensitivity to Iodine as a Cause of Periarteritis Nodosa, Bull. Johns Hopkins Hosp. **77**:43, 1945.
26. Marine, D., and Baumann, E. J.: Periarteritis Nodosa-like Lesions in Rats Fed Thiouracil, Arch. Path. **39**:325, 1945.
27. Karsner, H. T.: Acute Inflammations of Arteries, Publication No. 6, American Lecture Series, Springfield, Ill., 1947, Charles C Thomas, Publisher.
28. Von Haun, F.: Patho-histologische und experimentalle Untersuchungen über Periarteritis Nodosa, Virchows Arch. f. path. Anat. **227**:90, 1919.
29. Harris, W. H.: Etiology and Pathology of Periarteritis Nodosa, South. M. J. **19**:426, 1926.
30. Arkin, A.: A Clinical and Pathological Study of Periarteritis Nodosa, Am. J. Path. **6**:401, 1930.

COARCTATION OF THE AORTA AT UNUSUAL SITES

Report of Two Cases With Angiocardiographic and Operative Findings

Henry T. Bahnson, M.D., Robert N. Cooley, M.D., and Robert D. Sloan, M.D.

Baltimore, Md.

IN A series of twenty-two patients with coarctation of the aorta subjected to angiocardiography before operative treatment, the usual finding by angiocardiography and at operation was a stenosis at the level of the ductus arteriosus. In two instances, however, the coarctation was demonstrated considerably distal to the usual site; in the midthoracic aorta in one patient and below the renal arteries in another. In order to clarify the syndrome associated with such lesions, we present summaries of the histories of these two patients.

CASE REPORTS

Case 1 (J.H.H. 447239).—B. A., a 35-year-old white woman, was admitted to the surgical service because of hypertension, exertional dyspnea, and numbness and stiffness of the legs. Seven years before admission a routine physical examination had disclosed hypertension. One year later, after running for a bus, the patient suddenly noted numbness and stiffness in both lower extremities. Subsequently the numbness and stiffness of the legs ensued after even mild exercise, and headaches and dizziness were noted. In 1944 the patient underwent bilateral supradiaphragmatic splanchnicectomy with removal of long segments of the greater splanchnic nerves as well as lesser and least splanchnic nerves. The blood pressure in the arms ranged around 230/110 before operation and 195/100 after operation. At that time absence of femoral pulsations was noted, but there was no evidence of collateral circulation and the existence of coarctation of the aorta could not be proved.[1] The headaches and dizziness disappeared, but numbness in the legs persisted. Later the headaches recurred, and in the year before entry the patient developed dyspnea on slight exertion, edema of the ankles, left-sided tinnitus, and transient attacks of amblyopia. She had ten attacks suggesting angina pectoris and began to sleep sitting up in an effort to prevent the severe morning headaches. From her local physician she learned that her blood pressure was slowly rising.

On this admission the systolic blood pressure ranged from 230 to 260 mm. Hg; the diastolic pressure ranged from 110 to 130. No blood pressure readings could be obtained in the lower extremities. There was slight increase in light-streaking of the retinal arteries. The scars of a bilateral paravertebral sympathectomy extended from the level of the sixth thoracic to the second lumbar vertebra. The heart was not enlarged. Over the base a systolic murmur was heard which was transmitted to the neck and back. A soft systolic murmur was heard over the back on either side; this was most intense at the tenth thoracic vertebra, where it became loud and harsh. A similar murmur was heard just below the xiphoid cartilage. Pulsations felt in the epigastrium could not with certainty be differentiated from the forceful cardiac impulse. The radial pulses

From the Departments of Surgery and Radiology, The Johns Hopkins University and the Johns Hopkins Hospital.

were full and equal; no pulsations were felt in the legs or in the lower abdomen. No unusual vascular pulsations were felt over the chest. A roentgenogram of the chest showed the heart to be of normal size. There was no evidence of notching of the ribs. The urine was normal. Twenty-five per cent of the injected phenolsulfonphthalein was excreted in fifteen minutes and 70 per cent in two hours. An oscillometric test in the left upper arm showed 7.0 mm. of oscillation at a pressure of 170 mm. of mercury. No oscillation could be obtained in either lower extremity.

The patient was admitted with the diagnosis of coarctation of the aorta. There was no doubt that she had aortic obstruction, but the level of the block was thought to be unusual because of the peculiar murmur, the epigastric pulsation, and the absence of collateral circulation in the chest wall despite the patient's age and the hypertension. Angiocardiography was performed with the patient recumbent in the left lateral position. The right ventricle, pulmonary artery, left auricle, and aorta appeared to be normal. There was no evidence of coarctation of the thoracic aorta. A similar injection technique with serial roentgenograms of the abdomen showed complete obstruction of the abdominal aorta at the level of the first lumbar vertebra just

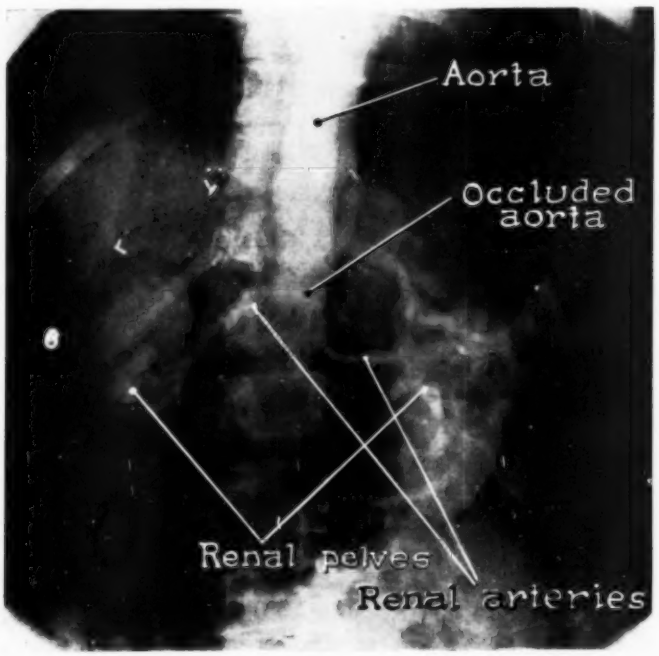


Fig. 1.—Case 1. Visualization of the abdominal aorta by angiocardiographic technique. The renal arteries and the obstruction of the aorta just above them are seen. The renal parenchyma is partially opaque from the Diodrast. Renal pelves are visualized because of a previous injection.

below the origin of the renal arteries (Fig. 1). The renal arteries were demonstrated. The aorta was slightly dilated above the occlusion, and in a conventional film was seen to be slightly more dense than normal, suggesting that there were arteriosclerotic changes. A film taken one second later showed the renal parenchyma to be opaque and of normal size and shape. The renal pelves were filled from the previous injection of Diodrast.

Studies by Bing, Campbell, Handelsman, and Griswold,[2] with techniques to be described, demonstrated a cardiac output of 3.9 liters per minute per square meter of body surface. Blood flow as measured by plethysmography was 4.6 c.c. per minute per 100 c.c. of tissue in the arm and 1.6 c.c. per minute in the leg. Normal values obtained by this method have ranged from 4.0 to 7.0 c.c. through either extremity. The blood pressure in the right brachial artery was more than 200 mm. Hg systolic and 100 mm. Hg diastolic, with a mean pressure of 144 by direct intravascular

measurement. A ureteral catheter inserted into the left femoral artery was passed to the aortic bifurcation at the level of the third lumbar vertebra. Pressure by direct measurement was 52/45, with a mean of 48 mm. of mercury.

Studies of renal function were performed by Genest using his customary techniques.[3] These showed a renal plasma flow of 690 c.c. and a glomerular filtration rate of 178 c.c. per minute per 1.73 square meters of body surface area. The filtration fraction was thus 0.259. This agrees with other investigations demonstrating that hypertensive patients with or without coarctation have evidence of constriction of the efferent arterioles and a resultant increase in the filtration fraction.

On Jan. 16, 1948, Dr. Alfred Blalock performed an exploratory laparotomy. It was thought that if the aortic obstruction were proximal to, or involved the origin of, the renal arteries, an anastomosis of the splenic to the renal artery would be beneficial. The arteries in the rectus abdominis muscles were more prominent than usual. For several inches below the diaphragm the aorta was two to three times normal size. Below this it tapered rapidly to become quite small at about the level of the second lumbar vertebra. Pulsations could not be felt in the arterial tree distal to this area. The lumen of the distal aorta was felt to be patent, but very little blood was flowing through it. The left renal artery was visualized throughout its course and was apparently slightly smaller than normal. The right renal artery was not visualized but could be felt to arise from the aorta just above the obstruction. An attempt was made to denervate the left renal artery by stripping its adventitia. The omentum was placed against the upper surface of the left kidney to aid in collateral circulation. The sympathetic chains together with the second, third, and fourth lumbar ganglia were removed on each side.

The postoperative course was uneventful. The legs were warmer and slight pulsations were felt in the femoral, popliteal, and dorsal pedal arteries. The patient's tolerance for walking was difficult to evaluate but seemed to be slightly improved. She was discharged on the twelfth postoperative day with slight relief from the complaints given on admission.

CASE 2 (J.H.H. 453317).—A. P., a 17-year-old white girl, was admitted to the surgical service because of hypertension discovered in a routine physical examination eight months before. She had noted frequent supraorbital headaches for fifteen months, but these seemed related to eyestrain and decreased in frequency after she stopped school work. She had been otherwise well and had been very active physically throughout her life.

Except for the cardiovascular system, the physical examination was normal. The retinal arteries were seen to be slightly narrowed. The heart was not enlarged; the rate was 100. A harsh, high-pitched, blowing, midsystolic murmur was heard over the entire precordium, loudest, in the second left intercostal space, and transmitted to the vessels of the neck and back. The blood pressure was 180/90 in both upper extremities; it was 145/120 in the left lower extremity and 140/100 in the right lower extremity. Pulsations in the interscapular region could not be felt with certainty. Radial pulses were bounding. Femoral pulses were weak and no pulses could be felt in the distal portions of the lower extremities. Studies of the urine and blood chemistry were normal. Thirty per cent of the injected phenolsulfonphthalein was excreted in fifteen minutes and 75 per cent in two hours.

Unpublished studies by Bing, Handelsman, Campbell, and Griswold showed the brachial arterial pressure to be more than 200 mm. Hg systolic and 100 diastolic. The right femoral arterial pressure was 90/61, with a mean of 78. The cardiac output was 6.7 liters per minute per square meter of body surface. The blood flow in the arm was 4.3 c.c. per minute per 100 c.c. of tissue, and 1.8 c.c. per minute per 100 c.c. of tissue in the leg.

A conventional roentgenogram of the chest showed no definite evidence of notching of the ribs. Angiocardiograms were at first thought to show a narrow band of constriction at the usual site just below the left subclavian artery. Subsequent to surgical exploration this was interpreted as a shadow cast by the bronchus of the left upper lobe (Fig. 2). Several centimeters distal to this point was a long area of narrowing, beyond which the aorta appeared smaller than normal.

On March 10, 1948, Dr. Alfred Blalock performed an exploratory thoracotomy. Incision was made for removal of the fifth rib. A moderate number of collateral vessels were encountered when the incision was made. The arch of the aorta was of normal size. The left subclavian artery was about twice the usual size but was not as large as that usually seen in cases of coarctation. There was no coarctation at the usual site in the region of the ductus arteriosus. However,

several intercostal spaces lower there was diminution in the size of the aorta over a distance of about 4.0 cm., in the center of which the lumen was felt to be quite small. The wall of the aorta in this region appeared to be thickened and indurated, especially on its posterolateral aspect. Distal to the 4.0 cm. area of constriction the aorta increased in size but never reached normal caliber. The intercostal arteries showed remarkably little increase in size. The lung was adherent along the involved segment of the aorta and there was no good plane of cleavage between the aorta and the surrounding tissues. The irregular, pebbly appearance of the aorta suggested an old inflammatory process (Fig. 3).

An attempt at correction of the coarctation would have required a free arterial graft since the area was too far caudad to permit use of the subclavian in the manner described by Blalock and Park.[4] A partial sympathectomy was performed, with removal of the sympathetic chain and ganglia from the second to the eleventh rib.

The patient's subsequent course was uncomplicated. When discharged from the hospital ten days after operation she was asymptomatic, with a blood pressure in the arms of 145/85.

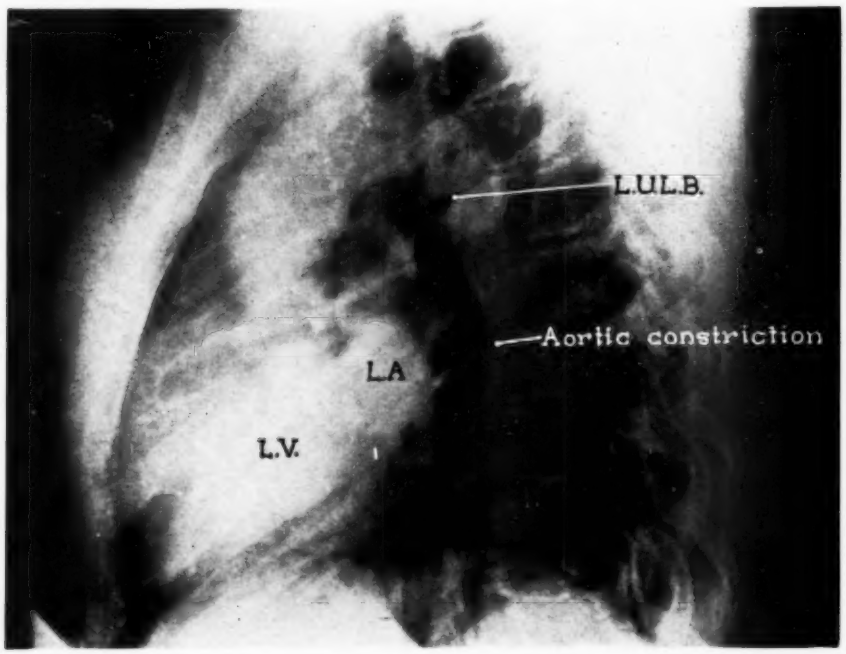


Fig. 2.—Case 2. Angiocardiogram showing the left side of the heart and aorta. The left auricle (*L.A.*), left ventricle (*L.V.*), and aorta are seen. The bronchus of the left upper lobe (*L.U.L.B.*) is responsible for the appearance of a constriction in the isthmic region of the aorta. The actual lesion was below this point.

DISCUSSION

Since the surgical treatment for coarctation of the aorta was introduced independently in 1945 by Crafoord[5] and by Gross,[6] the value of such therapy in certain cases has become established. Most cases of coarctation of the aorta fall into two poorly defined groups[7,8]: (1) The so-called "infantile" type, in which the stenosis is diffuse in the arch of the aorta and customarily between the left subclavian artery and the ductus arteriosus. There are usually significant cardiac defects. Such a condition is almost always incompatible with life for

Fig. 3.—Case 2. Drawing demonstrating the diffuse narrowing below the region of the obliterated ductus arteriosus. The surrounding adhesions are shown.

more than a few days or weeks. (2) The "adult" type, in which the stenosis is localized at or just below the ductus arteriosus, which is partially or totally obliterated. There is usually no other cardiac defect, except possibly a bicuspid aortic valve. Patients with this latter type of aortic defect survive to adult life and are possible subjects for surgical excision of the stenotic area. A rare third type has been described in which the stenosis is below the region of the ductus arteriosus.[9-19]

In recent years there has been increased awareness of this disease on the part of diagnosticians. Though easily diagnosed, it is readily overlooked. The syndrome may include a history of vascular insufficiency in the lower extremities and symptoms of hypertension. The diagnostic signs include absent or diminished arterial pulsations in the lower extremities, a blood pressure lower in the legs than in the arms, evidence of collateral circulation over the thorax, and notching of ribs as seen in the roentgenograms. Although hypertension in the arms and upper part of the body is not invariably present, it is usually a significant feature and not infrequently is the presenting complaint.

These diagnostic observations indicate an obstruction to the flow of blood in the aorta between the vessels to the arms and those to the legs. The level of the obstruction cannot be localized accurately by routine clinical methods. In most patients requiring operation, preoperative determination of the exact site of constriction is not necessary, for it is rare that a patient with the infantile type of this disease reaches adult life or becomes a candidate for operation. Excepting this group of patients, the coarctation in almost all other instances might be assumed to lie in the region of the obliterated ductus arteriosus. However, the two cases described in this report suggest that an accurate localization of the constriction is not only helpful but essential before surgical exploration.

Angiocardiography has been performed in this hospital in an effort to determine before operation the degree and the level of the constriction. Many of these patients have been referred from the Cardiac Clinic at the Harriet Lane Home of the Johns Hopkins Hospital. A modification[20] of the method described by Robb and Steinberg[21] has been used. Interpretation of such roentgenograms is often difficult because of the many overlying shadows in the region of the aortic arch, but the degree and the level of coarctation as well as the distance between the origin of the left subclavian artery and the site of constriction can be estimated. It is the latter point which determines the choice between excision of the stenotic area with end-to-end anastomosis and employment of the left subclavian artery to by-pass the coarctation, as described by Blalock and Park.[4] It is important to know the level of coarctation in selecting the rib for removal since the operative approach should be as direct as possible to avoid dividing more collateral vessels than necessary.

From the available literature we have collected ten cases in which there was an aortic stenosis below the region of the ductus arteriosus. These cases are apparently of two different types; when the stenosis is above the diaphragm the constriction is more diffuse, while the subdiaphragmatic stenoses are usually localized at or just below the level of the renal arteries. Such a classification at present has little significance, although the appearance of the lesion suggests a different etiological basis in the two types.

The first case of stenosis of the thoracic aorta below the region of the ductus arteriosus was reported by Schlesinger[9] in 1835. In this patient, who died of cardiac failure, the upper aorta was aneurysmal. Just above the diaphragm the aorta was so small as scarcely to allow the passage of a small sound; below the diaphragm the aorta was normal. Hasler[10] in 1911 reported a patient in whom the aorta abruptly became completely obliterated 3.0 cm. above the diaphragm. A fibrous cord 7.0 mm. in diameter replaced the aorta over 2.5 cm. of its thoracic portion. Costa[11] in 1931 reported a patient who died following rupture of the first intercostal artery. There was a stenosing diaphragm in the aorta between the first and second intercostal arteries. This is the only recorded case in which the low-lying thoracic stenosis is so sharply localized, and more closely resembles the usual type of coarctation in the isthmus. Also in 1931, Hickl[12] reported a case with cylindrical narrowing of the thoracic aorta just below the isthmus. He attributed this to meso-aortitis but had no proof of the etiological factor. From his description and illustration, the gross pathologic change seems to resemble that in others of this group. Hahn[13] in 1933 described a patient who died as a result of hypertension and cardiac failure. At the level of the diaphragmatic dome there was a marked constriction through which only a 3.0 mm. sound could be passed. The aorta elsewhere was normal for the age of the patient. Schleckat[14] subsequently reported the same case.

Power[15] in 1861 reported the first case of stenosis of the abdominal aorta below the origin of the visceral arteries. The iliac branches were correspondingly small. Maycock[16] collected all cases reported prior to 1936 and included a patient with protracted amebic dysentery who had brachial arterial hypertension and in whom autopsy demonstrated a complete obliteration of the aorta 1.5 cm. below the origin of the renal arteries. There were gross degenerative changes in the aorta proximal to the stenosis, while below it remained "very delicate and well preserved." Baylin[17] in 1939 described a 32-year-old subject encountered during an anatomic dissection in the course of which complete obstruction of the aorta just distal to the orifices of the renal arteries was observed. He attributed the obstruction to calcification in the walls of aneurysmal dilatations, two of which lay anteriorly just below the renal arteries, with a larger dilatation posteriorly slightly below the first two. The obstruction occurred between the first two and the third, at the level of the second pair of lumbar arteries. Immediately above and below the dilatations there were calcium deposits in the wall, but elsewhere the aorta was completely free of changes.

Steele[18] reported extensive clinical studies performed upon a patient who had hypertension in the arms while the legs showed a low systolic but an elevated diastolic pressure. At autopsy there was constriction of the aorta just above and at the level of the renal arteries. The lumen of the aorta was reduced to about 2.0 mm. in size. Steele[19] has recently studied a patient in whom a thoracolumbar sympathectomy had previously been performed for hypertension. Angiocardiograms made by Dr. George P. Robb showed constriction of the abdominal aorta for about four inches, being immediately below the diaphragm; the aorta and its branches proximal to the isthmus were increased in size, while the isthmus and the descending aorta were uniformly decreased in caliber.

The origin of this condition is obscure, but several theories have been advanced. Hasler[10] felt that the thoracic stenosis was due to an acquired disease but could find no histologic evidence of syphilis, neoplasm, or scar and concluded that an organized thrombus of unknown origin was the cause of the narrowing. Costa[11] suggested implants of embryonic aortic arches as the cause of all types of coarctation. He felt that the pre-isthmic stenosis was due to a remnant of the fifth arch; the isthmic type, to a remnant of the sixth; and that which he described just below the first intercostal artery, to a remnant of the right aortic arch. Hickl[12] related the diffuse thoracic stenosis to rheumatic fever but without convincing evidence. He also mentioned syphilis as a possible cause of the stenosis, but the stenosis in each of the other cases he cited was in the isthmic region and the syphilis might have been incidental to the usual type of coarctation. Schleckat[14] felt that the condition was embryologic in origin since he could find no evidence of an inflammatory genesis. Maycock[16] believed that the abdominal stenosis which he described was due to a congenital developmental defect and suggested that the condition might be due to changes involving unequal fusion of the two dorsal aortas with obliteration and loss of one of them.

Relatively little can be said concerning the etiological factors of the two cases reported here when considered in relation to reports which include gross and microscopic pathologic data. There was no history or clinical evidence of syphilis or rheumatic fever in either of these patients. The difference in appearance of the involved areas was impressive. The stenosis in the thoracic aorta was diffuse and the surrounding thickening and irregularity of the aortic wall suggested a low-grade chronic inflammatory change, possibly embryonic or neonatal. The abdominal stenosis, on the other hand, was sharply localized and did not suggest inflammation. It is possible that the thoracic and abdominal aortic stenoses represent the same disease process at different stages in development. The sharp contrast in the anatomic lesions, however, suggests that the pathogenesis of the two conditions is different. In most reported cases of diffuse narrowing the lesion is located in the thoracic aorta, while the abdominal coarctations are more sharply localized. The cases of Costa[11] and of Steele[19] provide exceptions to this generalization.

We believe that the abdominal stenosis reported here was of long duration and probably congenital, although the abrupt onset of symptoms related to the deficient circulation of the lower extremities suggested thrombosis of a previously narrowed segment of the aorta. That the abdominal stenosis in our patient could have been secondary to thrombosis or embolism of the aorta was considered, since occlusion without symptoms has been reported.[22,23] Such patients, however, have suffered from other disease processes which were not present in this patient. The relationship of coarctation to hypertension is not clear, but this patient (B. A.) had hypertension before symptoms of deficient circulation to the legs appeared.

SUMMARY

1. Coarctation at an unusual site in the thoracic aorta of one patient and in the abdominal aorta of another has been demonstrated by angiocardiography and at operation.

2. It is felt that the occurrence of aortic obstruction at such unusual sites, though admittedly rare, nonetheless provides a strong argument for routine use of angiocardiography preliminary to surgical treatment of coarctation.

3. Ten similar cases collected from the literature are reviewed and discussed from the standpoint of the etiological basis. Although proof of any theory is lacking, it is felt that the stenosis in such instances is a congenital lesion.

4. Thoracic and abdominal aortic constriction would appear to have a different though possibly related pathogenesis.

REFERENCES

1. Peet, Max M.: Personal communication, May, 1948.
2. Bing, R. J., Handelsman, J. C., Campbell, J. A., Griswold, H. E., and Blalock, A.: The Surgical Treatment and Physiopathology of Coarctation of the Aorta, Ann. Surg. **128**:803, 1948.
3. Genest, J., Newman, E. V., Kattus, A. A., Sinclair-Smith, B., and Genecin, A.: Renal Function Before and After Surgical Resection of Coarctation of the Aorta, Bull. Johns Hopkins Hosp. **83**:429, 1948.
4. Blalock, A., and Park, E. A.: Surgical Treatment of Experimental Coarctation (Atresia) of the Aorta, Ann. Surg. **119**:445, 1944.
5. Crafoord, C., and Nylin, G.: Congenital Coarctation of the Aorta and Its Surgical Treatment, J. Thoracic Surg. **14**:347, 1945.
6. Gross, R. E., and Hufnagel, C. A.: Coarctation of the Aorta; Experimental Studies Regarding Its Surgical Correction, New England J. Med. **233**:287, 1945.
7. Taussig, H. B.: Congenical Malformations of the Heart, New York, 1947, The Commonwealth Fund, p. 618.
8. Reifenstein, G. H., Levine, S. A., and Gross, R. E.: Coarctation of the Aorta. A Review of 104 Autopsied Cases of the "Adult Type," 2 Years of Age or Older, Am. Heart J. **33**:146, 1947.
9. Schlesinger: Merkwürdige Verschliessung der Aorta, Casper's Wchnschr. f. d. ges. Heilk. No. 31, p. 489, 1835.
10. Hasler, L. H.: Über einen Fall von Verschluss der Aorta an ungewohnter Stelle. Inaug. Diss., Borna-Leipzig, 1911, R. Noske.
11. Costa, A.: Obliterazione dell'aorta all'imbocco dell'aorta destra; rottura della prima intercostale aortica. Classificazione e patogenesi delle atresie e stretture dell'aorta, Arch. di pat. e clin. med. **9**:305, 1930.
12. Hickl, W.: Über zylindrische Aortenverengerung im absteigenden Brustteil infolge von Mesoaortitis, Frankfurt, Ztschr. f. Path. **41**:176, 1931.
13. Hahn, M.: Zur Frage tiefsitzender Stenosen der absteigenden Brustaorta, Inaug. Diss., Berlin, 1933.
14. Schleckat, O.: Angeborene ringförmige Stenose der Aorta descendens in Zwerchfellhöhe, Ztschr. f. Kreislaufforsch. **25**:417, 1933.
15. Power, J. H.: Observations on Diseases of the Aortic Valves, Producing Both Constriction of the Aortic Orifice and Regurgitation Through It Into the Left Ventricle, Accompanied With Abnormal Enlargement of the Two Internal Mammary Arteries and Atrophy of Abdominal Aorta and Its Iliac Branches, Dublin Quart. J. Med. Sc. **32**:314, 1861.
16. Maycock, W. d'A.: Congenital Stenosis of the Abdominal Aorta, Am. Heart J. **13**:633, 1937.
17. Baylin, G. J.: Collateral Circulation Following an Obstruction of the Abdominal Aorta, Anat. Rec. **75**:405, 1939.
18. Steele, J. M.: Evidence for General Distribution of Peripheral Resistance in Coarctation of the Aorta: Report of Three Cases, J. Clin. Investigation **20**:473, 1941.
19. Steele, J. M.: Personal communication, May, 1948.
20. Cooley, R. N., Bahnson, H. T., and Hanlon, C. R.: Angiocardiography in Congenital Heart Disease of Cyanotic Type With Pulmonic Stenosis or Atresia. I. Observations on the Tetralogy of Fallot and "Pseudo-Truncus Arteriosus," Radiology **52**:329, 1949.
21. Robb, G. P., and Steinberg, I.: Visualization of the Chambers of the Heart, the Pulmonary Circulation, and the Great Blood Vessels in Man, A Practical Method, Am. J. Roentgenol. **41**:1, 1939.
22. Gross, H., and Phillips, B.: Complete Occlusion of the Abdominal Aorta. A Review of Seven Cases, Am. J. M. Sc. **200**:203, 1940.
23. Greenfield, I.: Thrombosis and Embolism of the Abdominal Aorta, Ann Int Med. **19**:656, 1943.

CONGENITAL MITRAL STENOSIS AND SYSTEMIC RIGHT VENTRICLE WITH ASSOCIATED PULMONARY VASCULAR CHANGES FRUSTRATING SURGICAL REPAIR OF PATENT DUCTUS ARTERIOSUS AND COARCTATION OF THE AORTA

HENRY SWAN, M.D., J. M. TRAPNELL, M.D., AND JOHN DENST, M.D.
DENVER, COLO.

CONGENITAL mitral stenosis is a rare cardiac anomaly. The exact incidence of this lesion is difficult to determine because the terms "stenosis," "atresia," and "aplasia" are not always used in the same sense by different authors. Quoting from Dorland[1] stenosis is "narrowing or stricture of a duct or canal"; atresia is "imperforation, absence, or closure of a normal opening"; and aplasia is "incomplete or defective development of tissue." Both congenital mitral stenosis and atresia are usually associated with aplasia of the left side of the heart and other developmental anomalies. We are presenting a case of congenital mitral stenosis in which the associated defects were all extracardiac, with the exception of right ventricular enlargement, and consisted of hypoplasia and coarctation of the aorta, a large patent ductus arteriosus, and an anomalous coronary artery.

From an extensive review of the literature, Donnally[2] was able to collect only eleven proved cases of congenital mitral stenosis, to which he added one of his own. In this series hypoplasia of the left side of the heart and enlargement of the right ventricle were the most constantly associated defects. The maximum duration of life was forty-two months. All of the patients developed cyanosis and dyspnea shortly after birth.

Abbott[3] in a statistical analysis of 1,000 cases of congenital cardiac disease listed six under mitral stenosis and five under atresia. The commonest defects associated with the former were patent ductus arteriosus, right ventricular hypertrophy, and hypoplasia of the left ventricle and ascending aorta. The oldest patient was 27 years of age.

Farber and Hubbard[4] described two cases of congenital mitral stenosis occurring in infants 36 and 72 hours old, which they attributed to a "fetal endomyocarditis." Bland, White, and Jones[5] cast some doubt on an inflammatory pathogenesis by stating that a minimum of two years is probably necessary for the development of any extensive valvular deformity.

Roberts[6] reported a case in a 20-hour-old infant associated with aortic atresia. He also stated that his was the tenth reported case showing aortic atresia with the usual combination of defects (mitral stenosis, left ventricular

From the Departments of Surgery, Medicine, and Pathology of the University of Colorado Medical Center.

hypoplasia, stenosis of ascending aorta and arch, patent foramen ovale, right ventricular and pulmonary artery dilatation and hypertrophy, enlarged ductus arteriosus, and nonpatent interventricular septum).

Morgan and Sprenkel[7] described a case of cor biventriculosum pseudotriloculare in which there was an "anomalous and stenotic mitral valve with cleft aortic leaflet." It is of interest that the patient lived to the age of 60 years.

Jacobius and Moore[8] reviewed 169 cases of congenital heart disease at the New York Hospital, and classified four as mitral stenosis. Field[9] listed a similar incidence of this lesion, reporting seven cases of stenosis out of a total of 250 cases of congenital heart diseases. The oldest patient in this series was 1 year and 9 months of age.

Clawson[10] added two more cases of mitral stenosis collected from a group of 141 cases of congenital heart deformities. One of these patients was a stillborn infant and the other died at the age of 9 months.

CASE REPORT

J. S., an 11-year-old white girl, was first seen in the Pediatric Clinic of Colorado General Hospital in August, 1940, complaining of lifelong exertional dyspnea and fatigability, frequent bouts of epistaxis and recurrent attacks of tonsilitis during the preceding six years. The patient's mother stated that she was told that her child had "heart disease" when the infant was 14 days old. The attacks of epistaxis were thought by the child's physician to have been episodes of rheumatic fever and digitalis had been given. There was no past history of chorea, or of cyanosis in the neonatal period. The family history was noncontributory. The patient was admitted for tonsillectomy.

Physical examination revealed slight malnourishment and underdevelopment for a child of 11 years. The temperature, pulse, and respiration were normal. The brachial blood pressure was 130/70. There was questionable cardiac enlargement. Murmurs were described by three different observers as follows: an apical systolic by one; a presystolic by another; and a presystolic with thrill plus a diastolic, both of maximum intensity in the fourth left intercostal space, by yet a third examiner. The extremities showed no evidence of cyanosis or clubbing.

A teleroentgenogram showed a globular-shaped heart with widening on the right and in the region of the thoracic aorta. The electrocardiogram was reported as being consistent with either rheumatic or congenital heart disease on the basis of a prominent P_2 and marked right axis deviation. Laboratory studies revealed a 1 plus albuminuria with an occasional formed element, a red blood cell count of 4.7 million with 14.1 gm. of hemoglobin, and normal bleeding and coagulation times.

Following uneventful tonsillectomy the child was discharged, to be followed in the outpatient department. The diagnosis lay between rheumatic heart disease with mitral stenosis and insufficiency, or congenital heart disease, type undetermined.

The patient was not observed again until July, 1945, when, at the age of 16, she was seen in the Rheumatic Fever Diagnostic Clinic at Colorado General Hospital, having been referred by the school physician. Interval history revealed increasing fatigability and weakness, particularly of the lower extremities, associated with muscle and joint pains but no definite arthritis. Menarche had occurred one year previously and the periods were still irregular.

On this examination the patient was found to be twenty-three pounds under her expected weight. The brachial blood pressure was 130/100. The heart was not enlarged to percussion. The pulmonic second sound was greater than the aortic and accentuated. There was a low-pitched, rough, rumbling systolic murmur of moderate intensity and a brief diastolic murmur, both localized to the pulmonic area. The femoral pulsations were normal and no cyanosis or clubbing of the extremities was noted.

The electrocardiogram was essentially unchanged from that taken five years previously. Cardiac fluoroscopy was of interest. The anterioposterior position demonstrated a tipped-up

apex suggestive of right ventricular enlargement, and a definite increase in the size of the pulmonary artery. The lung markings appeared dense, but no "hilar dance" was noted. In the left anterior oblique position the posterior contour cleared the vertebral column normally. In the right anterior oblique position the left auricle was thought not to be enlarged. Laboratory studies now revealed a polycythemia as manifested by a red cell count of 5.8 million, hemoglobin of 19 Gm., and a hematocrit of 75. The sedimentation rate was normal and the urinalysis showed no abnormality.

The impression at that time was that the patient had congenital heart disease, the most probable lesion being an interauricular septal defect.

She was readmitted to the hospital for further diagnostic studies in October, 1946. She now gave a history of intermittent claudication and also complained of frequent headaches with associated visual disturbances.

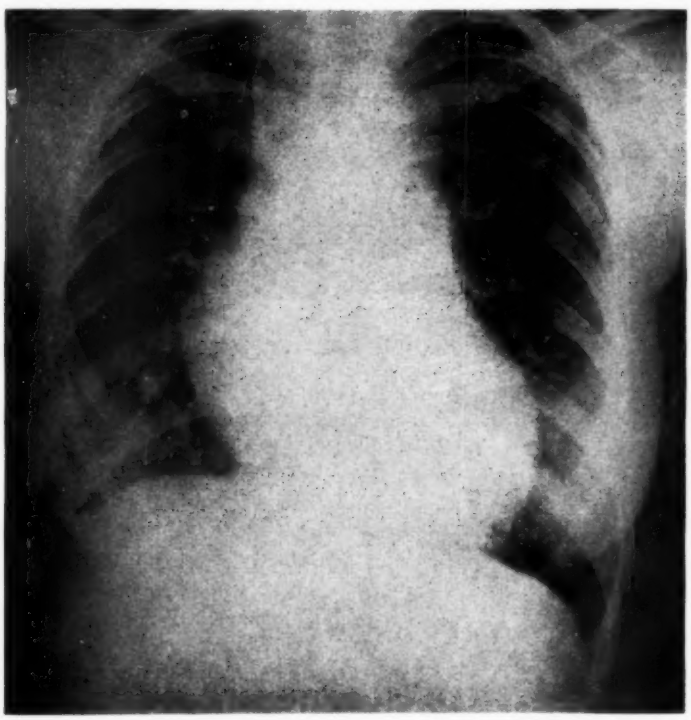


Fig. 1.—X-ray film of the heart and lungs taken Dec. 2, 1947, showing the prominence of the right ventricle, the pulmonary conus, and the congestion of the lung fields.

On physical examination it was noted that *the toes were clubbed and cyanotic but the fingers were normal in color and configuration.* The blood pressure was found to be consistently higher in the upper than in the lower extremities with transient rises to hypertensive levels; for example, 129-160/90-118 in the right arm and 105/85 in the right leg. There was marked cupping of the optic discs (later diagnosed as juvenile glaucoma). The lungs were clear to percussion and auscultation. A Grade 3 systolic murmur was heard at the pulmonic area with transmission upward. No diastolic murmur was noted. The liver edge was palpable 3.5 cm. below the right costal margin. There was a palpably enlarged pulsating vessel in the midscapular region. The radial artery pulsations were felt to be stronger than those in the femoral artery.

Laboratory studies again showed a polycythemia with a red blood cell count of 7.1 million and a hemoglobin of 17 grams. Circulation times for arm-to-lung with ether were 5 seconds and 13.5 seconds on two trials; the arm-to-tongue time with Decholin was 21 seconds and 25 seconds on two tests.

Chest x-ray films demonstrated enlargement of the transverse diameter of the heart due mainly to accentuation of the right border, congestive changes in both lung fields, and the presence of a probable azygos lobe. The ribs were not notched. Fluoroscopy of the heart again showed a prominent pulmonary artery and enlarged right auricle and ventricle without demonstrable left auricular enlargement. The electrocardiogram was unchanged. A phonocardiogram showed a late systolic murmur and a split second-sound.

The impression at this point was that the patient had a coarctation of the aorta with an associated interauricular septal defect. Because of postoperative ocular complications, which followed surgery for glaucoma, additional diagnostic studies of her cardiac lesion were not undertaken until a year later, when she was 18 years of age.

For several months prior to readmission to the hospital in September, 1947, the patient had noted increasing dyspnea and orthopnea, together with intermittent pedal edema. She also complained of frequent "fainting spells" which were usually preceded by a feeling of extreme weakness.

The blood pressure in the left arm was 140/120 and in the left leg 120/100. There was a Grade 3 systolic murmur along the left sternal border and a definite diastolic murmur over the pulmonic area. The liver was enlarged 3 to 4 cm. below the right costal margin. By x-ray examination, the contour of the heart was unchanged (Fig. 1).

The percentage oxygen saturation of the arterial blood in the dorsalis pedis artery was 69.3, that in the radial artery was 94.

The possibility of a large patent ductus arteriosus with a right-to-left shunt distal to the coarctation was now considered. As the patient responded well to routine therapy for cardiac decompensation, it was possible subsequently to perform catheterization of the right side of the heart. This procedure was carried out to obtain further evidence on the cardiac circulation with particular reference to the presence or absence of a septal defect. Blood samples and pressure recordings were taken from the right auricle and ventricle and from the right femoral and left brachial arteries. An attempt to advance the catheter into the pulmonary artery was unsuccessful. The pertinent findings obtained from these catheterization studies are shown in Table I.

TABLE I. RESULTS OF CATHETERIZATION AND BLOOD PRESSURE STUDIES

LOCATION	OXYGEN SATURATION (PER CENT)	PRESSURE (STRAIN GAUGE) (MM. HG)
Right auricle	52.6	
Right ventricle	46.2	
Brachial artery	92.1	130/90
Femoral artery	70.2	68/40

From these results it was concluded that the patient did *not* have an interauricular septal defect, and that approximately one-half of the blood in the femoral artery was coming from the right ventricle, presumably through a large patent ductus entering below a coarctation.

The patient's problem was thoroughly discussed in our Chest Conference. There was uniform agreement that the diagnosis was coarctation of the aorta, probably of the infantile type, with a large patent ductus arteriosus entering the aorta distal to it. The abnormal hemodynamics was discussed and most of the consultants felt that the chief strain on the heart was due to the increased load on the right ventricle because of the patent ductus. It seemed apparent that a large percentage of the output of the right ventricle was flowing through the ductus into the aorta at a pressure measured at the femoral artery of 68/40. It was felt that closure of the ductus would tend to remove this strain on the right side of the heart, but at the same time, because of the coarctation, additional strain might be placed on the left ventricle. If repair of the coarctation could be accomplished at the same time, it was hoped that the hemodynamics might be restored to normal. Whether the patient could tolerate occlusion of the aorta during the procedure was questioned, but in the last analysis it was clear that her heart was beginning to fail with increasing rapidity, and her prognosis without surgery was extremely grave.

Preparations for operation were elaborate. Because of the extreme viscosity of her blood (hematocrit of 76) it was felt that less work would be required of her myocardium during operation if the blood were made more fluid. This was accomplished by serial small venesections during the week preceding surgery. Her hematocrit was reduced from 76 to 61, the hemoglobin from 18 Gm. to 15 Gm., and the red cell count from 8.0 million to 6.25 million.

It was felt desirable to be able to evaluate and take immediate corrective measures against any undesirable alterations in her hemodynamics during the operative procedure. A medical-physiological team of five men was present throughout the procedure. With needles in the right radial artery, the right antecubital vein, and the left femoral artery, they were prepared to inject or withdraw blood or fluid from either side of the vascular circuit as indications arose. Constant arterial and venous pressure recordings were taken with the strain gauge. These preparations were made under Avertin anesthesia.

Endotracheal ether anesthesia was begun, and through an anterolateral thoracic incision the mediastinum was entered and the great vessels exposed. A very large pulmonary artery was found from which led a patent ductus arteriosus 2.0 cm. in diameter to the descending aorta. For a distance of about 1.0 cm. above the entrance of the ductus the aorta was extremely small in caliber, perhaps 0.6 cm. in diameter. It was slightly larger, but still definitely smaller than normal (1.0 cm.) between the origins of the left subclavian artery and the left common carotid artery. The first four intercostal arteries were much enlarged. A thrill was palpable in the descending aorta but none in the pulmonary artery *and none over the surface of the heart.* Temporary occlusion of the ductus caused no alteration in the patient's condition as reflected in her chart. It was decided to ligate the ductus as the initial step, with the idea in mind of then proceeding to resection of the coarctation if the patient's condition remained satisfactory. In further freeing the ductus a small tear was made inferiorly which complicated the application of the clamps on the ductus. The hemorrhage was estimated at about 300 c.c. of blood, which was replaced into the femoral artery. Closure of the pulmonary side of the ductus proceeded without event, save that there was an increasing tendency to bleed through the needle holes as we proceeded. It was the operator's impression that the pulmonary artery pressure was rising rapidly during this procedure.

The patient's condition remained quite stable to this point, which was approximately one-half hour after occlusion of the ductus. Respirations, however, suddenly ceased, followed in about one minute with cessation of the cardiac beat. Massage, artificial respiration, transfusion, and stimulants were without avail, and the patient was declared dead. The venous pressure began to rise just before cessation of the heart beat.

Pathologic Findings.—The body was that of a well-developed and well-nourished white girl 18 years of age, measuring 164 cm. (64.5 inches) long and weighing 43.6 kg. (96 lb.). The toes showed advanced clubbing, and the fingers were normal. The autopsy incision was limited to the operative wound of the thorax. The anatomic findings of chief interest were hypoplasia of the aortic arch and coarctation, a ductus arteriosus (Fig. 2), an unusual form of mitral stenosis, an anomalous coronary circulation, and structural changes in the branches of the pulmonary arteries.

The heart weighed about 400 grams and the ventricles were contracted. The left ventricle was normal in size. The right ventricle was hypertrophied so that the two ventricles were approximately equal. The walls measured 10.0 mm. on the left and 9.0 mm. on the right. The left atrium, which was dilated to about twice the normal size, had a wall 5.0 mm. thick. The right atrium was mildly dilated and the wall was slightly hypertrophic. The interauricular septum showed no defect. The mitral valve was unique (Fig. 3). The atrioventricular ring measured 3.0 cm. in diameter. The valve itself consisted of a peripheral shelf of thin gray tissue, 5.0 to 10.0 mm. wide, which showed no trace of the commissures nor the formation of separate cusps. The chordae tendineae were shortened and fused to form a funnel-shaped, firmly fixed, almost solid sheet of tissue that obstructed the orifice of the valve. This anomalous septum was perforated by fifteen scattered slitlike openings, measuring from 1.0 to 5.0 by 2.0 mm. in diameter. The blended chordae were inserted into the apex of the solitary, double-bellied papillary muscle, which arose from the posterior wall of the left ventricle near the margin of the intact interventricular septum. Viewed from above, the mitral valve resembled the inverted top of a salt shaker. The tricuspid, pulmonic, and aortic valves appeared normal.

Microscopically, the epicardium and the endocardium were normal. The myofibers of both ventricles and of the left atrium were enlarged, and the nuclei were plump and vesicular. The interstitial connective tissue was scanty, with no lesions suggesting rheumatic fever. There was no fatty degeneration of the myocardium.

The aorta was thin-walled and the intima was smooth. The ascending aorta measured 2.0 cm. in diameter, but distal to the disproportionately large innominate artery, the aortic arch narrowed to 1.1 cm. in diameter. Distal to the origin of the left common carotid artery, the arch further narrowed to 8.0 mm. in diameter. A segment of the aorta, 8.0 mm. long, and situated immediately distal to the origin of the left subclavian artery, showed coarctation. This segment measured 6.0 mm. in external diameter, and the lumen was completely obstructed at one point by a thin membranous partition. The ductus arteriosus had been completely resected:

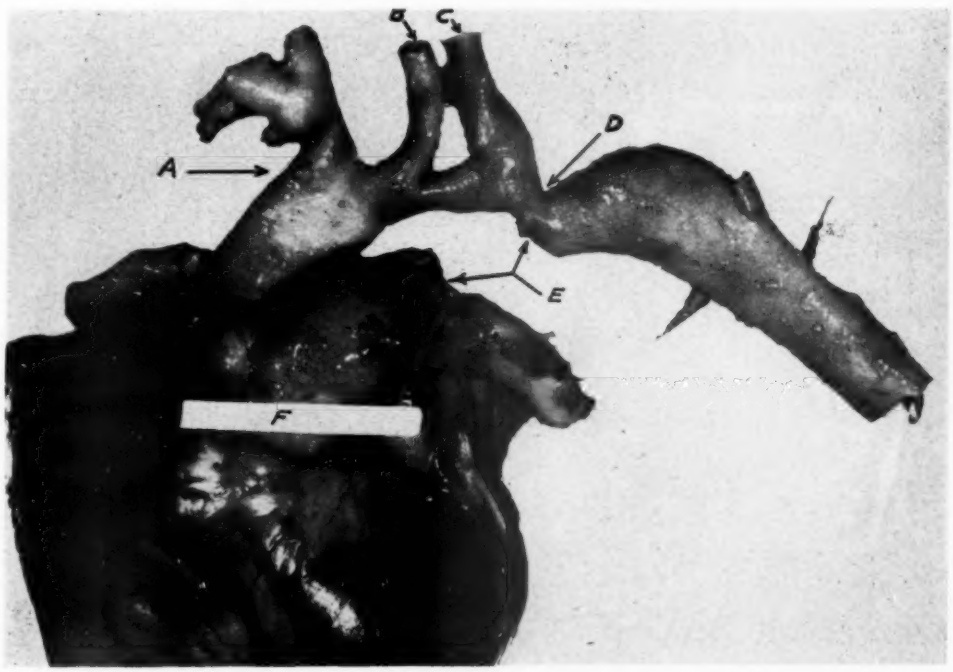


Fig. 2.—Photograph of the heart and great vessels. The hypoplasia of the aortic arch, the large pulmonary artery, and the surgically ligated stumps of the patent ductus arteriosus are evident. *A*, Innominate artery; *B*, left common carotid artery; *C*, left subclavian artery; *D*, coarctation; *E*, ligated stumps of the patent ductus arteriosus; *F*, pulmonary artery.

one end opened into the pulmonary artery near the base of the left pulmonary artery superiorly, the opposite end of the ductus entered the descending aorta. Just distal to the area of coarctation and atresia, the descending aorta abruptly expanded to 1.5 cm. in diameter. The enlarged innominate, left common carotid, and left subclavian arteries measured 12.0 mm., 7.0 mm., and 9.0 mm. in diameter, respectively, at the points of origin. The intercostal arteries also were enlarged The pulmonary artery measured 2.3 cm. in diameter.

Microscopically, the walls of the constricted portion of the aorta and of the pulmonary artery were not different from those of normal great vessels.

The right coronary artery and the anterior descending branch of the left coronary artery arose from normal positions in the sinuses of Valsalva, but the caliber of each vessel was minute and did not exceed 2.0 mm. in the most proximal portions. The left circumflex branch was absent. The most important coronary artery was an anomalous vessel measuring 5.0 mm. in diameter

which originated from the posterior wall of the pulmonary artery near the bifurcation of that vessel. It coursed over the free tip of the left atrial appendage and descended along the left border of the heart to the apex.

Microscopically, the adventitia and media of each coronary vessel appeared normal and the intima was thin.

Grossly, the lungs were dark red, crepitant, and moist. The main interest lay in the microscopic examination. The pleura and interlobular septa were edematous, the alveolar walls were hyperemic, and many of the alveoli contained precipitated edema fluid and macrophages. The

Fig. 3.—Anterior view of the opened left ventricle, showing the funnel-shaped mitral valve cut radially. The few slitlike openings are formed by the irregular fusion of the coarse chordae tendinae which insert on the single papillary muscle.

latter contained no iron pigment. The pathologic alterations of the walls of all of the small arteries and larger arterioles were impressive (Fig. 4). The media showed advanced hypertrophy, and the adventitia was thick and collagenous. Sections stained for elastic tissue demonstrated coarsening and splitting of the internal elastic membrane and extensive proliferation of irregularly arranged elastic fibers throughout the media. Focal areas of the media were also fibrosed. Many of the small arteries exhibited diffuse or eccentric fibrocellular thickening of the intima, with partial obstruction and, in a few instances, obliteration of the lumens. In those arteries showing the

heaviest intimal fibrosis, the elastic tissue in focal areas of the wall was atrophic or absent, while a meshwork of fine and coarse elastic fibers was retained in other areas of the wall. The lumen of a single large artery was almost occluded by an organized mass of connective tissue. The walls of the smallest arterioles were usually thin, but the internal elastic membrane of some was thickened and split.

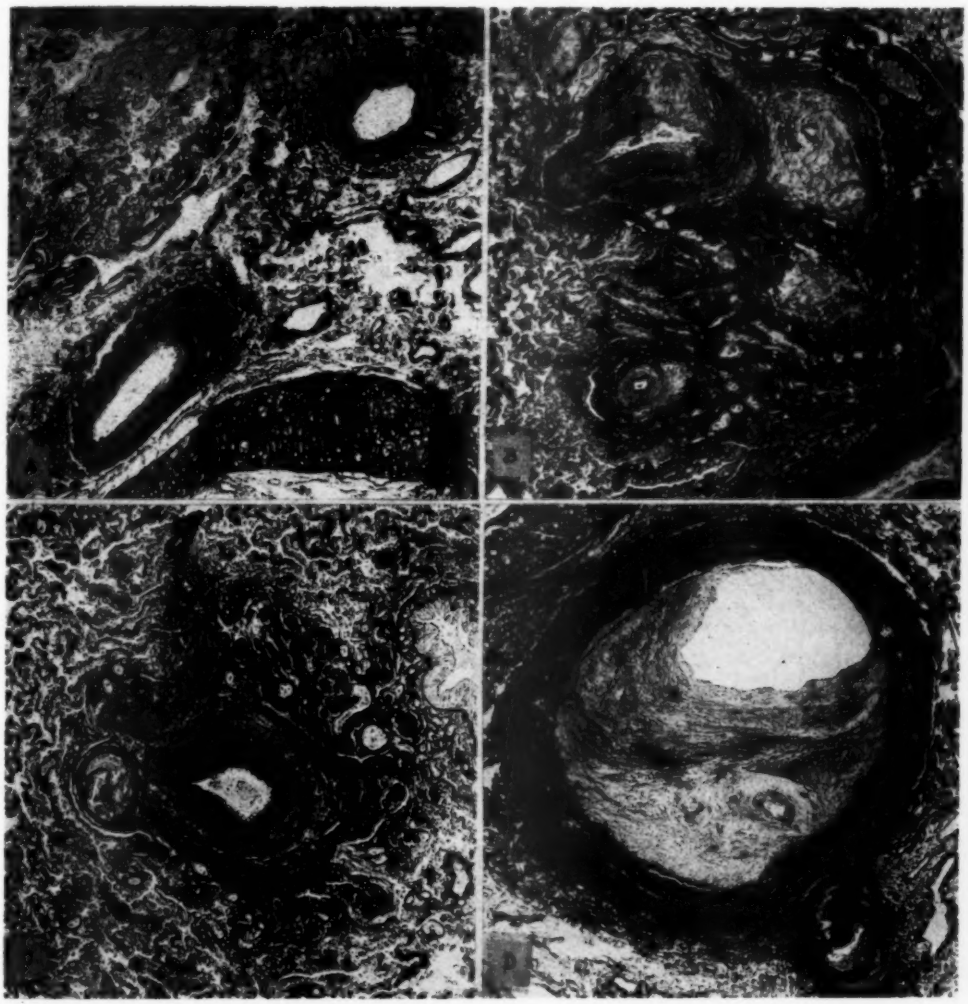


Fig. 4.—Photomicrographs of the pulmonary arterial tree. (Elastic tissue stain, X 60). *A*, Small arteries showing hypertrophy of the media and hyperplasia of elastic tissue. *B*, Group of small arteries showing obliterative advanced fibrosis of the wall and irregular distribution of elastic tissue. *C*, A small artery showing medial and adventitial fibrosis with irregular proliferation of elastic tissue in the media. *D*, A medium-sized artery showing obstruction of the lumen by organized connective tissue.

DISCUSSION

The left ventricle in this patient appeared normal in size, but the hypoplasia of the aortic arch was severe, and the progressive diminution of the caliber of this vessel, proximal to the opening of the ductus arteriosus, indicated an infantile type of coarctation. The septum traversing the lumen of the aorta in the area of the coarctation completed the obstruction to the flow of oxygenated blood from the arch into the descending aorta. The great vessels branching from the aortic arch were enlarged to accommodate the increased blood flow from the left ventricle into the head and upper extremities, and to supply the only oxygenated blood to the descending aorta via the collateral circulation. If the segment of coarctation had been successfully resected along with the ductus arteriosus, the flow of oxygenated blood to the trunk and lower extremity might not have been greatly improved because of the hypoplasia of the rest of the aortic arch.

The origin of the mitral stenosis was undoubtedly congenital, because gross and microscopic stigmas of rheumatic heart disease or other forms of endocarditis were absent. The term "mitral stenosis" is used, for the want of a more descriptive name, and, furthermore, the valve itself did not resemble that associated with rheumatic fever. The hemodynamics resulting from the obstructive valvular lesion probably differed from the type accompanying rheumatic mitral stenosis in that regurgitation was apparently minimal, while obstruction was apparently as great as was compatible with life.

The changes in the medium-sized and small ramifications of the pulmonary artery were widespread and severe. It is not unlikely that the first alteration in the pathogenesis of these lesions, as suggested by Edwards,[11] was hypertrophy of the media of the small vessels. The extensive proliferation of the elastic fibers, the fibrosis of the intima, and the obstruction of the lumen may have occurred subsequently. This is borne out by the comparison of these lesions with those observed by Douglas, Burchell, and Edwards[12] in a child afflicted with what was aptly termed a "systemic right ventricle." The physiologic advantage of the organic changes in the small vessels, in order to maintain the pulmonary hypertension necessary to direct a large proportion of the blood from the pulmonary artery into the descending aorta, is obvious.

Clearly, the ductus arteriosus was a principal outlet for much of the blood leaving the right ventricle, and it was supplying approximately one-half of the blood to the trunk and lower extremities. When the ductus was ligated, the blood which it had previously carried was suddenly channeled into the pulmonary artery. Either the narrowed pulmonary vascular bed or the stenotic mitral valve, or both, were incapable of transmitting the suddenly increased volume. Blood, therefore, was dammed back into the right chambers of the heart; the pressures in the right chambers increased until failure of the myocardium led to death. We believe, from this experience, that in a patient with a systemic right ventricle, conversion of the hemodynamics to normal may be impossible if the changes in the pulmonary vascular bed have progressed to an advanced stage.

In the re-evaluation of this case, we attempted to find a clue which would have led to the preoperative diagnosis of the lesion of the mitral valve. The

physical examination was confusing because the heart murmurs were inconstant, and a murmur diagnostic, or even suggestive, of mitral stenosis was not heard. The fluoroscopic examination failed to reveal the enlargement of the left atrium. The electrocardiographic findings of a prominent P wave and severe right axis deviation were not helpful, as little importance was attached to them in the presence of aortic coarctation and a patent ductus arteriosus. We were unable, in retrospect, to understand how the diagnosis of mitral stenosis could have been established.

Had the diagnosis been made, however, the operation would not have been undertaken. The preoperative rationale of the surgical attempt was based on the opinion that the patient had only two abnormalities, patent ductus and coarctation, both of which individually are amenable to surgical correction. It was then hoped that it might be possible to restore the hemodynamics to normal by correction of the lesions when occurring in this combination. Moreover, observation of the patient's course over the past two years left little room for doubt as to the prognosis if she were not treated.

SUMMARY

The clinical and pathologic findings in a girl 18 years of age suffering from multiple congenital cardiovascular defects are presented. A previously undescribed form of mitral stenosis was associated with coarctation of the aorta and a patent ductus arteriosus. The necessity for establishing the preoperative diagnosis of intracardiac lesions when they are combined with lesions of the great vessels which are potentially amenable to surgical correction is discussed. Of especial importance were the advanced changes in the pulmonary arterial system associated with the systemic right ventricle. Operative restoration of normal hemodynamics may not be possible in the presence of systemic right ventricle if advanced pulmonary vascular changes are present.

REFERENCES

1. Dorland, W. A. N.: The American Illustrated Medical Dictionary, ed. 21, Philadelphia, 1947, W. B. Saunders Company.
2. Donnally, H. H.: Congenital Mitral Stenosis, J. A. M. A. **82**:1318, 1924.
3. Abbott, M.: Congenital Heart Disease, Nelson's Loose Leaf Living Medicine **4**:207, 1931.
4. Farber, S., and Hubbard, J.: Fetal Endomyocarditis: Intrauterine Infection as the Cause of Congenital Cardiac Anomalies, Am. J. M. Sc. **186**:705, 1933.
5. Bland, E. F., White, P. D., and Jones, T. D.: The Development of Mitral Stenosis in Young People, AM. HEART J. **10**:995, 1935.
6. Roberts, J. T.: A Case of Congenital Aortic Atresia and Hypoplasia of Ascending Aorta, Normal Origin of the Coronary Arteries, Left Ventricular Hypoplasia and Mitral Stenosis, AM. HEART J. **12**:448, 1936.
7. Morgan, D. R., and Sprenkel, V.: Cor Biventriculosum Pseudotriloculare, J. Tech. Methods **16**:18, 1936.
8. Jacobius, H. L., and Moore, R. A.: Incidence of Congenital Cardiac Anomalies in the Autopsies at the New York Hospital, J. Tech. Methods **18**:133, 1938.
9. Field, C. E.: Congenital Mitral Stenosis, Arch. Dis. Childhood **13**:371, 1938.
10. Clawson, B. J.: Types of Congenital Heart Disease in 15,597 Autopsies, Lancet **64**:134, 1944.
11. Edwards, J. E.: Personal communication.
12. Douglas, J. M., Burchell, H. B., and Edwards, J. E.: Systemic Right Ventricle in Patent Ductus Arteriosus: Report of a Case With Obstructive Pulmonary Vascular Lesions, Proc. Staff Meet., Mayo Clin. **22**:413, 1947.

Abstracts and Reviews

Selected Abstracts

Mufson, I.: A New Treatment for the Relief of Obliterative Disease of Peripheral Arteries. Ann. Int. Med. **29**:903 (Nov.), 1948.

By means of a sphygmomanometer and rubber bulb, connected through a Y tube with an infusion burette, the author was able to introduce, under pressure, into the femoral artery in the affected limb a solution of histamine consisting of 1.0 mg. of histamine base in 500 c.c. of normal saline. The dropping rate was measured in the drip indicator during the diastolic fall in pressure during which inflow into the artery took place. It was found that between two and five drops per heart beat permitted an erythema of the thigh to develop without any subjective symptoms. The infusion was given at weekly or biweekly intervals, depending on the severity of the symptoms.

A total of seventeen patients were thus treated. Of this number, thirteen had symptoms of intermittent claudication and four suffered from muscle cramps during sleep. Local alterations of blood flow before and after treatment were predicated upon measurements of skin temperature and the diffusion rate of radioactive sodium over the sole of the foot and the calf following the introduction of 100 microcuries of radioactive sodium into the median basilic vein. Aside from increments in local blood flow, a significant increase in walking tolerance was noted in approximately 80 per cent of those who were disabled because of claudication. The proportions of those with arteriosclerosis obliterans and thromboangiitis obliterans, respectively, are not given. Of the four patients with night cramps, complete abolition of this symptom was accomplished in every instance by three to six weekly infusions of the histamine solution.

The author considers this type of therapy the equivalent of a sympathectomy in a physiological sense and, therefore, recommends its use as a substitute for surgical management of peripheral vascular disease.

WENDKOS.

LaDue, J. S., Murison, P. J., and Pack, G. T.: The Use of Tetraethylammonium Bromide as a Diagnostic Test for Pheochromocytoma. Ann. Int. Med. **29**:914 (Nov.), 1948.

A benign pheochromocytoma of the right adrenal gland, weighing 298 grams and containing over 8.0 grams of epinephrine, was successfully removed from a 41-year-old man who had suffered from crises of hypertension and episodes of nervousness, palpitation, sweating, throbbing headache, and abdominal pains. Pyelograms had demonstrated downward displacement of the superior pole of the right kidney by an extrarenal mass. The blood cholesterol was 441 mg. and the blood sugar 134 mg. per cent.

Striking elevations of the arterial blood pressure could be induced, prior to operation, by one of the following methods: (a) by having the patient lie on his left side and raise his shoulder by leaning on his left arm; (b) by intravenous injection of 2.0 c.c. of a saline solution containing 0.025 mg. of histamine phosphate; (c) by intravenous injection of a solution containing 400 mg. of tetraethylammonium bromide. The mechanism responsible for the rise in blood pressure, provoked by the last-named procedure is not well understood and is still a matter of conjecture.

WENDKOS.

Bettman, R. B., and Tannenbaum, W. J.: Herniation of the Heart. Ann. Surg. **128**:1012 (Nov.), 1948.

The authors report a case of herniation of the heart through a pericardial defect. The pericardial defect resulted from the excision of an adherent piece of parietal pericardium in a patient in whom a pneumonectomy had been performed for carcinoma of the left lung. Following the pneumonectomy the patient was placed on his left side. He immediately went into shock. On reopening of the patient's chest, the heart was found herniated through the pericardial defect. The pericardial rim was slit and the heart was replaced. Recurrence was prevented by removal of practically the entire anterior pericardium. BECK.

Eichna, L. W.: Thermal Gradients During Varying Body Temperatures. Arch. Phys. Med. **29**:687 (Nov.), 1948.

The author studied the effect of the application of cold to the skin of patients with noninfectious fever. Patients were divided into two types: Those with a cool, either moist or dry skin; and those with a hot, and usually dry, skin. The author believes that the patient with the hot skin has a good blood flow to the skin and hence presents a good prospect for the lowering of the deep tissue temperature through the application of cooling agents to the skin. The vasoconstricting action of the cold will not be as effective in the case of the patient with a cool skin, since the cutaneous vessels are already vasoconstricted. The author found that even in the presence of cutaneous vasodilatation, cold agents applied to the skin are still likely to produce vasoconstriction and decrease the skin flow to the point where little heat is extracted directly from the blood by the cold. Under such circumstances there was a fall in peripheral tissue temperature with little or no decrease in rectal temperature. Attempts to maintain the cutaneous blood flow during the period of active cooling by friction of the skin were only partially successful in promoting a rapid lowering of rectal temperature during the cooling. The maximum cooling effect was obtained after the cooling agent was removed and the cutaneous circulation returned to its previous level. The author suggests that the most effective method of applying external cold would be in short repeated bouts rather than for long sustained periods.

In unfavorable instances, rectal temperature remains almost unchanged both during and after skin cooling. The vasoconstrictor reflexes initiated by the cool skin may outweigh the central vasodilating influence of the warm blood, and hence the skin remains relatively bloodless, the blood is not cooled, and the deep heat is not extracted. At times the reflexes from the cold skin are so strong that the patient chills and his body temperature may even rise.

ABRAMSON.

Holden, W. D.: Aortic Embolism. Arch. Surg. **57**:613 (Nov.), 1948.

After discussing the review of the subject of peripheral arterial embolism made by McClure and Harkins in 1943, the author presents the case history of a 58-year-old man in whom this operation was performed and discusses the autopsy findings in detail.

The early clinical recognition of acute occlusion of the abdominal aorta is not difficult if an examination of the pulses in the lower extremities is performed. The author stresses the importance of early diagnosis and early surgical intervention and discusses the main difficulties encountered in the successful treatment of peripheral arterial embolism.

BECK.

Herring, A. C., and Davis, W. M.: Penicillin Treatment of Subacute Bacterial Endocarditis: Report of Eighteen Consecutive Cases. J. A. M. A. **138**:726 (Nov.) 6, 1948.

An analysis is presented of eighteen unselected cases of subacute bacterial endocarditis treated with penicillin during the two-year period of 1944 and 1945. The predisposing cardiac abnormality was rheumatic fever in eleven patients, congenital heart disease in three, and arteriosclerosis in two; in two patients the underlying cardiac lesion could not be determined. In sixteen of the patients the causative organism was the *Streptococcus viridans*; an undifferentiated streptococcus and a pleomorphic streptococcus were isolated in the other two.

Penicillin was administered by either continuous intravenous or continuous intramuscular drip in a total dosage varying from 2,800,000 to 1,114,020,000 units. Heparin was used concomitantly in nine of the patients, three of whom developed febrile and systemic reactions thought to be due to the drug.

The infection was arrested in thirteen of the patients; treatment failures occurred in four patients; and one died during the course of therapy. Ten patients were alive and well one year or more after completion of treatment. All the treatment failures occurred in patients in whom infection had existed for longer than six weeks before therapy was instituted and in those patients in whom the penicillin sensitivity of the causative organism was more than 0.03 unit per cubic centimeter.

The authors point out that the only method of determining the effectiveness of treatment is a period of observation at the end of a course of penicillin. When relapse occurred, evidences became manifest within two weeks following cessation of therapy.

A daily dosage of at least 2,000,000 units of penicillin over a period of six weeks is recommended, and a daily dose of 5,000,000 units or more is advocated if the penicillin sensitivity of the organism is greater than 0.06 unit per cubic centimeter. The routine use of heparin in conjunction with penicillin is not recommended. HANNO.

Wilson, M. G., and Lubschez, R.: Longevity in Rheumatic Fever: Based on the Experience of 1042 Children Observed Over a Period of Thirty Years. J. A. M. A. **138:**794 (Nov. 13), 1948.

This paper presents a statistical analysis of the records of 1,042 children with rheumatic fever who were observed over the thirty-year period from 1916 to 1947. Eleven per cent of the patients disappeared from observation during the study. The average length of observation of the 89 per cent who were followed to death or until the end of the study was 14.8 years.

The mean age at onset of the initial rheumatic episode was 6.5 years. During the period of observation, the disease was characterized by active carditis alone in 7 per cent of the patients, by one or more attacks of chorea in 25 per cent, by polyarthritis with or without chorea in 58 per cent, and by active carditis in association with other rheumatic manifestations in 45 per cent. At last observation, cardiac involvement was demonstrable in every patient, and multiple valvular lesions and marked or decided cardiac enlargement were noted in about one-half of the patients. In about one-third of the group the auscultatory signs of valvular lesions regressed during the period of observation. Auricular fibrillation occurred in 4 per cent of the patients; fewer than one-half of the patients with auricular fibrillation survived until the end of the study. Ninety per cent of the group between the ages of 21 and 42 years were able to carry on their normal activity without circulatory embarrassment.

There were 226 deaths, an over-all death rate of 14.7 per 1,000 per year. Rheumatic heart disease accounted for 75.7 per cent of the fatalities and subacute bacterial endocartitis for 10.2 per cent. The over-all incidence of subacute bacterial endocarditis in the entire group was 2.2 per cent. The highest mortality rate took place within one year of onset of the initial attack, and an increased risk occurred at puberty, irrespective of the age at onset. The highest death rates occurred between the ages of 1 and 4 years (33.2 per 1,000) and 10 and 14 years (16.3 per 1,000). There was no significant sex difference in the age-specific mortality rates.

The median duration of life for rheumatic children is greater than thirty years after onset, and the over-all chance to survive to the age of 40 years is one out of two. From the age at onset, the fifteen-year survival rate is 80 per cent, the twenty-year survival rate is 75 per cent, and the thirty-year survival rate is 66 per cent. HANNO.

Meads, M., Long, R. U., Pace, S. H., and Harrell, G. T.: Caronamide and Penicillin: Serum Levels in Human Beings, Following Multiple Doses of the Drugs. J. A. M. A. **138:**874 (Nov. 20), 1948.

By virtue of its ability to alter the specific renal tubular enzyme system responsible for the excretion of penicillin, Caronamide (4′-carboxyphenylmethanesulfonanilide), although itself eliminated exclusively by glomerular filtration, retards the excretion of penicillin and enhances and prolongs the concentration of penicillin in the blood.

Seventeen subjects under 60 years of age, none of whom presented evidences of cardiac, renal, or hepatic dysfunction, were given 100,000 units of crystalline penicillin G intramuscularly every four hours for seven days, and Caronamide was simultaneously administered orally every four hours on the second, third, and fourth days. Blood samples were taken for penicillin and

Caronamide concentration determinations on each of the first four days and on the seventh day of the study. Seven of the patients (Group A) received Caronamide in a dosage of 2.0 Gm. every four hours, and ten (five each in Groups B and C) received the drug in rations of 4.0 Gm. every four hours. Determinations of the blood levels of Caronamide and penicillin were made four hours after the administration of the drugs in Groups A and B, and two hours after administration in Group C.

The enhancing effect of a given dosage of Caronamide on the penicillin concentration in the blood varied in different patients in the same group. Three of the seven patients receiving the 2.0 Gm. dose of Caronamide showed no significant increase in the penicillin level as compared with the control periods; in the remaining four patients in Group A intermittent twofold and fourfold increases in the level of penicillin occurred after two or three days of combined therapy. In those subjects receiving Caronamide in doses of 4.0 Gm., a twofold to seventeen fold enhancement of the penicillin level was noted, a greater degree of augmentation being noted two hours after the combined administration (Group C) than four hours after administration (Group B). Maximum penicillin concentrations were achieved after two days of combined therapy. A cumulative effect was noted with Caronamide during the three-day period of administration. The penicillin and Caronamide concentrations in the blood showed generally parallel changes. A blood Caronamide level of 25 mg. per cent was generally required to effect a twofold increase in the penicillin concentration; Caronamide levels exceeding 30 mg. per cent were necessary to increase the penicillin concentration fourfold or more.

No toxic effects from Caronamide were noted in the present study except for nausea in three subjects and vomiting in one. It is pointed out, however, that the toxicity of the drug has not as yet been completely evaluated and that other investigators have reported a rash, evidences of renal damage, and the appearance of a periarteritis nodosa-like syndrome.

Caronamide, because of its penicillin-enhancing effect, will probably prove to be of use in cases where high blood penicillin concentrations are required, such as the treatment of infections due to organisms of low penicillin susceptibility or organisms which have become penicillin resistant. HANNO.

Rosenburg, M. J.: Subacute Bacterial Endocarditis: Report of a Case of Reinfection. J. A. M. A. **138**:956 (Nov. 27), 1948.

A 31-year-old man was treated for subacute bacterial endocarditis, due to *Streptococcus viridans*, with 800,000 units of penicillin daily for six weeks and apparent cure was effected. After twenty months of good health, he again presented himself with the clinical picture of subacute bacterial endocarditis. Blood cultures again recovered the *S. viridans*, and in vitro tests showed the organism to be sensitive to less than 0.1 unit of penicillin per cubic centimeter. An apical abscess of a molar tooth was found, and culture of the abscess fluid after dental extraction yielded *S. viridans*. The patient was successfully treated with a total of 132,000,000 units of penicillin administered by the intramuscular route, every two hours, over a period of thirty-five days, and he has remained well during a five-month follow-up.

Because of the sensitivity of the causative organism to penicillin in the second attack of endocarditis, the long period of good health between the two episodes, and the presence of an abscessed tooth which apparently served as the site of origin of the second infection, the author believes that the second episode of bacterial endocarditis represented a reinfection rather than a relapse. HANNO.

Brust, A. A., Assali, N. S., and Ferris, E. B.: The Evaluation of Neurogenic and Humoral Factors in Blood Pressure Maintenance in Normal and Toxemic Pregnancy Using Tetraethylammonium Chloride. J. Clin. Investigation **27**:717 (Nov.), 1948.

In a series of twenty-three patients with toxemia of pregnancy and ten normal patients with pregnancies at term studied by the tetraethylammonium chloride (TEAC) "floor" blood pressure responses, it was found that in normal persons at term, the TEAC blood pressure floor is strikingly low and rises to normal levels after delivery. In patients with toxemia of pregnancy the TEAC floor is higher than normal and consistently falls to normal levels after recovery.

Since TEAC is known to eliminate neurogenic tone by blocking the automonic nervous system at the ganglionic level but has no effect on humoral tone, these results suggest that the hypertension in the toxemia of pregnancy is maintained by an excessive degree of humoral tone. In a normal pregnancy, it is likely that the neurogenic mechanisms are more active than in pregnancy with toxemia.

In general, the height of the TEAC floor parallels the severity of the toxemia. However, there is no evidence that TEAC can differentiate between toxemia and essential hypertension when influenced by pregnancy. It may have diagnostic possibilities in the study of those pregnant patients admitted with borderline elevations of blood pressure. Such patients who have a TEAC response resulting in a diastolic blood pressure floor considerably below 90 mm. Hg would be unlikely to have toxemia. WAIFE.

Stead, W. W., Reiser, M. F., Rapoport, S., and Ferris, E. B.: The Effect of Sodium Chloride Depletion on Blood Pressure and Tetraethylammonium Chloride Response in Hypertension. J. Clin. Investigation **27**:766 (Nov.), 1948.

In five patients with benign essential hypertension whose renal function was well preserved, the humoral component of the peripheral resistance (as reflected by the tetraethylammonium chloride "floor") was altered by changes in the salt balance. These patients were able to conserve sodium chloride and maintain a relatively isotonic concentration in the blood even against vigorous attempts at sodium depletion. In seven patients with hypertension who had either severe renal damage or malignant hypertension, the humoral contribution to the elevated blood pressure (the TEAC floor) was not altered by shifting of the sodium balance. In this latter group, a fall of 15 to 20 mEq. per liter of serum sodium concentration was associated with no fall in random pressure or the TEAC floor.

The authors conclude that in some patients with essential hypertension and normal renal function, sodium deprivation tends to decrease the humoral contribution to the maintenance of increased peripheral resistance. In patients with malignant hypertension, renal failure, or both, a large humoral component in peripheral resistance may be uninfluenced by an even greater degree of sodium depletion. WAIFE.

Briggs, A. P., Fowell, D. M., Hamilton, W. F., Remington, J. W., Wheeler, N. C., and Winslow, J. A.: Renal and Circulatory Factors in the Edema Formation of Congestive Heart Failure. J. Clin. Investigation **6**:810 (Nov.), 1948.

A total of thirty-nine patients, twenty-one in congestive failure and eighteen well-compensated, were studied to determine renal and circulatory factors in congestive heart failure. The right heart was catheterized and cardiac output measured. Whole blood volume was determined by the Evans blue dye method instead of by the more customary method of determining plasma volume and interpolating total blood volume from hematocrit. Sodium thiosulfate clearance was used to measure glomerular filtration. Other determinants were the sodium thiocyanate space and serum sodium. It was found that the thiocyanate space was definitely greater in uncompensated than in compensated patients. Furthermore, the kidneys of compensated persons were able to excrete sodium at nearly twice the rate of patients who were uncompensated, although the standard errors of the analyses were large because of the variability of the data. Changes of the blood volume were inconsistent and the averages of the two groups were not different.

The filling pressures of the right ventricle were higher in uncompensated than in recompensated patients. However, the pressure did not always decrease as compensation was regained nor was there any definite correlation between the height of the pressure and the thiocyanate space. There was little statistical difference between the means of the pressure of both uncompensated and compensated patients. Two patients were in congestive failure with high cardiac outputs. Including these subjects, the average output was higher in the compensated than in the uncompensated, but there was considerable overlapping and compensation was not necessarily accompanied by an increase in output.

Sodium resorption correlated closely with filtration rate. The authors explained this correlation by the manner in which the figures are derived; the amount of sodium resorbed is calculated by subtracting the quantity eliminated from the amount filtered. Since urinary sodium

is relatively a small quantity, changes here cause negligible changes in the amount filtered. The amount of sodium filtered is obtained by multiplying the plasma level (which is held within narrow limits) by the filtration rate. Thus, plotting sodium resorbed against filtration rate is not unlike plotting filtration rate against filtration rate times a constant. However, the ability to excrete sodium consistently improved as the patient regained compensation. These data confirmed the findings of others, that filtration rate in cardiac patients is much less than in normal subjects, but it is emphasized that patients can regain clinical compensation without a significant degree of increase in filtration rate. The ability to excrete sodium always increased after the compensation had been regained.

The determination which bore the closest relation between compensated and uncompensated patients was the oxygen saturation of mixed venous blood. The authors suggest that it is likely that the edema in congestive heart failure is formed from water which cannot be excreted and which is stored in the extravascular spaces. The inability of the kidney to get rid of edema fluid is due to overworking of the mechanism which resorbs salt and water and this in turn seems to be closely related to cellular hypoxia.

They found no support for the observation that an excess of hydrostatic over osmotic pressure in capillaries is a primary factor in the production of edema. Right auricular pressure, though higher than normal, was not consistently higher in the uncompensated than in the compensated patients.

The authors conclude that the circulatory disturbance of congestive failure produces a reduced oxygen tension in the mixed venous blood and that this brings about in some way a more complete resorption of salt and water by the kidneys which in turn is responsible for the edema.

WAIFE.

Salassa, R. M., Bollman, J. L., and Dry, T. J.: The Effect of Para-Aminobenzoic Acid on the Metabolism and Excretion of Salicylate. J. Lab. & Clin. Med. **33**:1393 (Nov.), 1948.

The effects of oral administration of para-aminobenzoic acid on the plasma salicylate level and on the urinary excretion of salicylates after oral administration of a single dose of sodium salicylate were studied in both men and dogs. The men were given 3.0 Gm. of sodium salicylate and blood samples were drawn at intervals over the next fifty-six hours. All urine passed during the remainder of the study was collected and the salicyl fractions were determined. When para-aminobenzoic acid was given, its administration was started eighteen hours before the ingestion of salicylate. Para-aminobenzoic acid, 3.0 Gm., was given every three hours for the duration of the study.

The authors found that after a 3.0 Gm. dose of sodium salicylate in men, the plasma salicylate level reached its peak of 18.0 to 22.0 mg. per 100 c.c. in two to four hours and then fell rapidly to 1.0 mg. or less per 100 c.c. in twenty-eight to thirty-two hours. However, when para-aminobenzoic acid was also given, the plasma salicylate level again reached its peak in two to four hours but fell more slowly. They found large quantities of salicyluric acid in the urine after the oral administration of the single dose of salicylate in man. However, when para-aminobenzoic acid was given with salicylates only very small quantities of salicyluric acid were found in the urine in spite of collection of the urine for a period of almost twice as long. There was no retention of salicyluric acid in the blood when it failed to appear in the urine as the plasma salicylate was practically all in the form of free salicylate and only the usual traces of salicyluric acid were present. In dogs the salicylate excretion was found to be much slower than in men and when para-aminobenzoic acid was given the rate of excretion of salicylate was not altered appreciably. Although the principle mechanism by which para-aminobenzoic acid increased the plasma salicylate level and decreased total salicylate excretion appeared to be the interruption of salicyluric acid formation, para-aminobenzoic acid also tended to lower the pH of the urine and this further decreased the total salicylate excretion by decreasing the renal clearance of the free salicylate fraction. When the urine was made strongly alkaline by massive doses of sodium bicarbonate, the clearance of free salicylate fraction increased and the effect of para-aminobenzoic acid was masked. Para-aminobenzoic acid when administered to man appeared to decrease greatly the formation of hippuric acid as measured by the oral hippuric acid liver function test.

KLINE.

Boyd, E. J., and Warner, E. D.: Effect of Vitamin K on Dicumarol-Induced Hypoprothrombinemia in Rats. J. Lab. & Clin. Med. 33:1431 (Nov.), 1948.

The purpose of this paper is to report the effect of Dicumarol on the prothrombin level of blood and the modification of that effect by vitamin K. The two-stage method of prothrombin determination was used. This method separates the conversion phase from the clotting phase and thereby eliminates the rate of conversion of prothrombin to thrombin as a factor in prothrombin measurement.

The authors found that when rats were given constant doses of Dicumarol there was a tendency for the animals to develop a tolerance to the drug. After approximately two weeks the prothrombin level tended to rise, and at the end of three to four weeks it commonly approached normal values. In another group of rats the dosage was gradually increased in an effort to keep the prothrombin at a low level. Although the prothrombin level tended to remain low for a longer time, the same effect was noted. Succeeding large doses had less effect than earlier small doses. The authors noted that the maximum hypoprothrombinemic effect of a single large dose of Dicumarol was attained within forty-eight hours and recovery was complete within ninety-six hours after the time of administration of the drug. Vitamin K in large doses had no detectable counteracting effect on the prothrombin level of rats whether given before, during, or after Dicumarol administration.

The authors believe that it is possible that administration of vitamin K affects factors which govern prothrombin conversion as well as those which control its concentration. This would explain the protective action of vitamin K against Dicumarol which has been reported by workers using the one-stage method of prothrombin estimation. It would also explain why this action is not demonstrable by the two-stage method.

KLINE.

Trimble, G. X.: Ventricular Irregularities Induced by Sympatho-Adrenal Discharge and Chloroform. J. Lab. & Clin. Med. 33:1438 (Nov.), 1948.

The authors present electrocardiographic studies on dogs in which a sympathoadrenal discharge was pharmacologically induced by the injection of acetylcholine bromide preceded by the injection of atropine and physostigmine salicylate. In this sequence of injections, presumably the muscarinic action of the acetylcholine is blocked by the atropine and the destructive action of cholinesterase on the acetylcholine held in check by the physostigmine, leaving the nicotinic action of the acetylcholine unrestrained. The nicotinic effects of acetylcholine are believed to include a sympathoadrenal discharge and the mobilization of epinephrine or an epinephrine-like substance. Following the series of injections, chloroform vapor was administered and continued uninterruptedly until a danger point was reached, as indicated by marked fall in blood pressure and apnea. Continuous electrocardiograms on Lead II, blood pressure, and respiration records were obtained from the time just prior to the acetylcholine administration until the cessation of the chloroform anesthesia. In six of the nine dogs studied, abnormal electrocardiographic findings were obtained during the reaction to chloroform. These consisted of ventricular extrasystoles, short runs of ventricular tachycardia, a persistent ventricular tachycardia of several minutes' duration, and a ventricular tachycardia changing to fibrillation during which the animal expired. These findings strengthen the suggestion of Chenoweth that intrinsic epinephrine, if liberated in sufficient quantity through emotional stress, could present a serious hazard through its effect on the ventricular complex sensitized to various lipotropic hydrocarbons.

KLINE.

Carson, M. J., Burford, T. H., Scott, W. G., and Goodfriend, J.: Diagnosis of Pulmonary Stenosis by Angiocardiography. J. Pediat. 33:525 (Nov.), 1948.

The authors describe their method for obtaining angiocardiograms by the use of the Tautograph, which makes ten radiographic exposures within a period of ten seconds. The normal configuration of the heart chambers and great vessels in the left anterior oblique and anteroposterior positions are presented in a series of figures. The radiograms of four patients with various types of cyanotic congenital heart disease are presented to illustrate the value of angiocardiography in

making the correct diagnosis. The cases presented included a nonfunctioning right ventricle with tricuspid stenosis, persistent truncus arteriosus, tetralogy of Fallot, and Eisenmenger's complex.

The authors feel that angiocardiography may be safely utilized as a diagnostic aid in many cardiac conditions especially in infants and children who are so small that cardiac catheterization is impossible or impractical. KLINE.

Irwin, H. R., and Winsor, T.: Venous Pressures in Children in Health and Disease. J. Pediat. **33**:556 (Nov.), 1948.

The subjects of this study were fifty children between the ages of 3 and 10 years with normal cardiovascular systems, thirteen children with rheumatic heart disease without evidence of congestive heart failure, and four children with glomerulonephritis, none of whom showed evidence of cardiac decompensation. In each subject the venous pressure was determined by the use of a phlebomanometer described by Burch and Winsor. From three to six consecutive readings were taken and the lowest pressure was recorded.

The authors found that in normal children the mean venous pressure between the ages of 3 and 10 years was 54.3 mm. H_2O, with a standard deviation of 17.1. They found that the venous pressure increased slightly with age. In patients with rheumatic heart disease without evidence of congestive failure the mean venous pressure was 92.7 mm. of water. In patients with acute glomerulonephritis the average venous pressure was 97.3 mm. of water.

KLINE.

Lubschez, R.: Immunologic and Biochemical Studies in Infants and Children With Special Reference to Rheumatic Fever. V. Electrophoretic Patterns in Blood Plasma and Serum in Normal Children. J. Pediat. **2**:570 (Nov.), 1948.

In this study the electrophoretic patterns of blood specimens from thirty apparently healthy children between the ages of 2 and 11 years are presented. There was no illness for a period of at least four months prior to sampling. The mean values for relative concentrations of the various components are in close agreement with those reported for adults. There were no significant sex differences. In younger children the albumen level was slightly higher and the gamma globulin level slightly lower. A second group of twenty-seven children with a mean age of 4.6 years is also presented. These children had had an illness within four months of the sampling. The illnesses comprised a wide variety of infections. In about 40 per cent of the determinations, there was an elevation of the gamma component. Sampling within a month of the illness produced the greatest number of abnormalities. JOHNSON.

Wilson, M. G., and Lubschez, R.: Immunologic and Biochemical Studies in Infants and Children With Special Reference to Rheumatic Fever. VI. Electrophoretic Patterns of Blood Plasma and Serum in Rheumatic Children. J. Pediat. **2**:577 (Nov.), 1948.

In rheumatic fever the observed increase in the gamma globulin fraction is sometimes offered as additional immunologic evidence of antecedent streptococcal infection, but the effect of antecedent illness has not usually been considered. In a study of the electrophoretic patterns of seventy-nine specimens from forty-two rheumatic children, the results were analyzed with respect to antecedent illness and rheumatic status. The electrophoretic patterns for rheumatic subjects who experienced neither an antecedent infection nor rheumatic fever were within normal limits. Those who developed rheumatic fever but had no antecedent respiratory infection did not demonstrate an increase in the gamma globulin component. Those with an antecedent respiratory infection, but no recurrence of rheumatic fever, showed significant elevations in the gamma component. Likewise, those with rheumatic fever developing subsequent to respiratory illness showed similar elevation of this fraction.

The observations recorded in this study demonstrate that the "elevation of the gamma globulin component is not a function of the rheumatic process but a reflection of previous infection." Apparently the rheumatic and the nonrheumatic subjects have a similar immunologic response to infections presumably streptococcal in origin. JOHNSON.

Kinmonth, J. B.: Thrombo-angiitis Obliterans. Results of Sympathectomy and Prognosis. Lancet **2**:717 (Nov. 6), 1948.

The author presents the results of a follow-up study on seventy-seven patients with proved thromboangiitis obliterans. Thrombosis of superficial veins had occurred in twenty-four. The series did not include an unduly high proportion of Jews. The average age of the patients at the onset of the disease was 35 years, the range being 16 to 48 years. The longest period between active episodes was found to be fourteen years. Of the seventy-seven patients, seven died after an average of 9.9 years following the onset of the disease. In each instance the cause of death was related to some type of vascular accident.

The author divided the patients into three groups according to their clinical manifestations. One group consisted of individuals in whom the onset of the disease was in the main vessels, as the femoral or popliteal. In these the predominant symptom was intermittent claudication in the calf, with pronounced postural color changes and wasting of the calf muscles. The collateral circulation was usually adequate to prevent gangrene of the foot and the skin was comparatively healthy. The second group consisted of those patients in whom the smaller vessels were the first to be attacked. Popliteal pulsations were present, but the pulses at the ankle were reduced or absent. The findings consisted of claudication in the sole, rest pain, constant erythrocyanosis of the skin and coldness, followed by ulceration or gangrene of the toes. Some of the patients had intermittent claudication in the calf, which, in the presence of pulsations in the popliteal artery was attributed to obstruction of the muscular branches of the main vessels. The third group consisted of patients with simultaneous involvement of both large and small vessels, with claudication in the calf, rest pain in the foot, and premonitory signs of gangrene.

Of fifty-six patients who had been sympathectomized, improvement in the extremities with regard to intermittent claudication was noted in twenty-five. The best results were found in the group with small vessel involvement. Of 111 patients who had been sympathectomized, the extremities of thirty-seven were amputated while those of seventy-four were preserved. The number of patients not sympathectomized was too small to compare with those on whom this operation was performed. Hence the value of sympathectomy in preserving the limb could not be ascertained. Furthermore, it was difficult to determine whether or not this procedure had any effect on stopping or slowing the progress of the disease. The author was of the opinion that sympathectomy was beneficial with regard to claudication in the sole, rest pain, and the superimposed vasospastic attacks characterized by coldness and numbless. In some of the patients with unilateral Buerger's disease in whom bilateral sympathectomy was performed, the disease subsequently appeared in what had been the sound limb. In other words, prophylactic sympathectomy died not give complete protection from the disease. ABRAMSON.

Wright, H. P., Osborn, S. B., and Edmonds, D. G.: Rate of Flow of Venous Blood in the Legs Measured With Radioactive Sodium. Lancet **255**:767 (Nov. 13), 1948.

Radioactive sodium was used to determine the rate of flow of venous blood up the leg in 121 normal people. The subject was placed in the supine position, a gamma-ray counter was arranged so that the screen lay transversely over the femoral vein in the groin, and 1.0 c.c. of the radioactive solution was injected into a prominent vein on the dorsum of the foot as rapidly as possible. Previously, a blood pressure cuff was placed over the ankle and the pressure raised in it to 40 mm. of mercury. The mean time taken for the material to reach the segment of femoral vein covered by the counter was found to be 18 ± 0.9 seconds, with an extreme range of observation of 4 to 50 seconds. ABRAMSON.

Harken, D. E., Ellis, L. B., Ware, P. F., and Norman, L. R.: The Surgical Treatment of Mitral Stenosis. Valvuloplasty. New England J. Med. **239**:801 (Nov. 25), 1948.

The authors discuss briefly the historical aspect of the surgical attack on the mitral valve in order to relieve mitral stenosis. The results in the past have been most discouraging.

A discussion is then carried out in regard to three groups of patients who might be benefited by one or another procedure to relieve the circulatory deficiency produced by the mitral stenosis. One of the procedures would be valvuloplasty, an attempt to relieve to some degree the stenosis of the thickened, diseased mitral valve and yet produce relatively minimal insufficiency.

In a second group of patients, there is a relative mitral regurgitation of greater significance than the stenosis, and in these patients, in whom there is a high pressure in the left auricle, the production of an artificial interatrial septal defect might be of value. The authors point out that this operation would not be suitable for patients who have experienced right ventricular failure.

In the third group, patients who are extremely ill and who have attacks of "hypercyanotic angina" are occasionally benefited by removal of the cardiac sympathetic accelerator and afferent nerves. This has been carried out by removal of the inferior cervical ganglion and the first four or five dorsal sympathetic ganglia.

The authors operated upon five patients with mitral stenosis. Two of them were subjected to valvuloplasty, two had atrial septal defects created, and one had cardiac denervation. There was one death and this occurred in the first patient on whom a valvuloplasty had been performed.

The authors point out four principles which they feel are important in the consideration of the surgical management of mitral stenosis:

1. The operation should be performed without dislocation of the heart from the position of optimum function.

2. The button-hole opening of the stenotic mitral valve should be approached from the auricular side so that the funnel directs the cutting instrument to the leaflet margin.

3. Surgical enlargement of the stenotic orifice should be so planned that there is minimal burden from the associated regurgitation (selected insufficiency), and maximum restoration of the valvular function (valvuloplasty).

4. In the presence of mitral obstruction or regurgitation, a rapid heart rate must be avoided; tachycardia tends to increase vascular pressure and is associated with attacks of pulmonary edema or "pulmonary decompensation."

The two patients upon whom valvuloplasty was performed are reported in detail.

LORD.

Palmer, J. L., and Gunderson, S. M.: The Effect of Dicumarol on the Erythrocyte Sedimentation Rate in Normal Men. New England J. Med. **239**:818 (Nov. 25), 1948.

Because of the dearth of information on the subject, the authors decided to test the effect of the drug on the sedimentation rate of normal persons. Five healthy medical students volunteered as subjects. All were free of a history of liver disease and of significant physical abnormalties.

On completion of these examinations, each subject was put on a daily dose of Dicumarol and daily prothrombin times were determined on the undiluted plasma of each. The prothrombin concentrations were maintained between 10 and 30 per cent of mean normal. The sedimentation rates were determined on twenty-one of the twenty-five days by the use of the Westergren method.

The results of this study indicate that Dicumarol administered in therapeutic dosage for twenty-five consecutive days has no significant effect on the erythrocyte sedimentation rate in normal men. It is possible that the results of this study cannot be applied to the interpretation of the effect of Dicumarol on the sedimentation rates of patients with associated diseases that are known to affect the sedimentation rate.

BELLET.

Gunther, B. S., and Concha, J B.: A New Method for the Electrical Recording of Mechanical Deformations. Proc. Soc. Exper. Biol. & Med. **69**:302 (Nov.), 1948.

The authors describe a new electrical method for recording mechanical variations. The method uses the differences in potential obtained by changes in the electrolytic resistance of a glass capillary filled with alcohol and glycerine. They recorded the following tracings obtained in man: (1) the carotid pulse, (2) the jugular pulse, (3) the venous pulse together with the R wave of the electrocardiogram, (4) the radial pulse and the R wave, and (5) the apex beat together with the R wave of the electrocardiogram.

KLINE.

Frisk, A. R., Hammarström, S., Lagerlof, H., Werkö, L., Björkenheim, G., Holmgren, A., and Larsson, Y.: Effect of Tetraethylammonium in Arterial Hypertension. Am. J. Med. 5:807 (Dec.), 1948.

Continuing their previous work, the authors have studied the effect of a standardized dose of tetraethylammonium (5.0 mg. per kilogram intravenously) on seventy-one hypertensive patients. The group was divided according to age and height of blood pressure. A comparison was made of the effect of tetraethylammonium upon blood pressure with the spontaneous variability of blood pressure during rest, and the influence of the drug on right auricular, ventricular, and pulmonary artery pressures, cardiac output, and the mean systemic pressure by intra-arterial blood pressure registration.

They found that in younger hypertensive patients without pronounced vascular changes, tetraethylammonium caused a moderate drop in both systolic and diastolic pressures corresponding to the lowest spontaneous value obtained during rest and sleep. In these patients, tetraethylammonium produced the relatively greatest increase in pulse rate. There was a marked lowering of the pressure in the lesser circulation to about one-half of the basic value. In older hypertensive patients with clinical signs of arteriosclerotic changes, tetraethylammonium produced the greatest drop in systolic pressure and relatively the least fall in diastolic pressure. In these cases the decrease in blood pressure fell below the lowest spontaneous value. They also showed the lowest average increase in pulse rate. Thus if administration of tetraethylammonium to a patient with hypertension produces a noticeable fall in systolic pressure and a relatively moderate drop in diastolic pressure simultaneously with a slight increase or decrease in the pulse rate, this is a sign of arteriosclerotic changes, and according to clinical experience, sympathectomy is of less value in these cases. They believe that the test is of some value in selecting patients suitable for operation. WOODS.

Rosenberg, B., Rosenthal, A. E., and Rosenbluth, M. B.: Effect of the Low Sodium Diet and the Rice Diet on Arterial Blood Pressure. Am. J. Med. 5:815 (Dec.), 1948.

This report is based upon observations in nine patients with essential hypertension in which a comparison was made between the findings obtained during the rice diet and during a diet low in sodium but adequate in protein. Each patient was studied in a control period averaging one month directly prior to institution of dietary therapy and for not less than four weeks while on the diet. Studies included blood pressure, urinary output, and blood and urinary sodium.

Case histories were presented and the following conclusions drawn: (1) Urinary sodium on both diets fell to very low levels, but the levels on the rice diet were lower than those on the low sodium diet. (2) Four of seven patients on the low sodium diet experienced a statistically significant fall in blood pressure while three of five on the rice diet did. (3) There was no relief of symptoms despite falls in blood pressure.

The authors believe that these changes are not of sufficiently significant magnitude to warrant the routine use of this type of therapy in the management of essential hypertension.

WOODS.

Steward, H. J., Shephard, E. M., and Horger, E. L.: Electrocardiographic Manifestations of Potassium Intoxication. Am. J. Med. 5:821 (Dec.), 1948.

The electrocardiographic manifestations of potassium are reviewed and two cases of potassium intoxication are presented. In these cases auricular standstill and widespread intraventricular block appeared in the electrocardiogram at a time when the serum potassium had risen to a level of 10.0 milliequivalents per liter or higher. In one case the changes followed administration of therapeutic amounts of potassium bicarbonate; in the other the changes occurred spontaneously in the course of the nephrotic stage of subacute glomerulonephritis. The latter represents the first reported case of death from potassium intoxication in the nephrotic stage of subacute glomerulonephritis with only moderate nitrogen retention.

It is recommended that potassium salts be administered with caution if there is any possibility of underlying renal disease. This is pertinent since many of the new salt substitutes contain appreciable amounts of potassium. Physiological saline solution and hypertonic glucose should be administered intravenously in the treatment of the cardiac manifestations of potassium intoxication. WOODS.

Book Reviews

TREATMENT OF HEART DISEASE. By William A. Brams, M.S., M.D., Ph.D., Associate Professor of Medicine, Northwestern University Medical School, and Attending Physician, Michael Reese Hospital, Chicago. Philadelphia and London, 1948. W. B. Saunders Company, 195 pages and 9 figures.

In publishing this monograph, Dr. Brams has succeeded in his stated purpose of providing a systematic and practical guide in the treatment of heart disease suitable for the general practitioner and medical student. An excellent review of the pharmacologic action of drugs used in the therapy of heart disease is presented in the first chapter. The discussion of therapy is inclusive, particularly that of congestive heart disease. The wide personal experience and mature judgment of the author is apparent throughout. The book is well written, the format is clear, and the bibliography is adequate.

H. K. HELLERSTEIN, M.D.

CORONARY HEART DISEASE. By A. Carlton Ernstene, M.D. Springfield, Illinois, 1948, Charles C Thomas, Publisher, 95 pages. Price $2.50.

This is a short monograph covering the entire subject of coronary heart disease from the clinical, electrocardiographic, and roentgenologic point of view. It deals with angina pectoris, myocardial infarction, acute coronary failure, and the complications and sequelae that may arise from these conditions. The book is well written and therefore easily read. Descriptions are excellent since there are no diagrams or figures to illustrate the points brought out. No matter how thoroughly one believes he understands this subject, it will no doubt be found profitable to again review it in this short, concise monograph.

JOSEPH A. WAGNER, M.D.

SUBACUTE BACTERIAL ENDOCARDITIS, Second Edition. By Emanuel Libman, M.D., and Charles K. Friedberg, M.D. New York, 1948, Oxford University Press, 116 pages and 19 figures. Price $3.50.

This book has been taken from the section on Subacute Bacterial Endocarditis in the Oxford Loose-Leaf Medicine and is a revision of the section published in 1941. The revision has been mainly directed toward the part on therapy. The advent of the new antibiotics, chiefly penicillin, has completely altered the prospects of a patient with subacute bacterial endocarditis. The discussion of their application is well presented in this volume and gives one a clear working knowledge of their uses.

The major part of the book is taken up with a detailed description of the pathology and clinical aspects of subacute bacterial endocarditis. Many original observations and concepts of the authors are presented. These are based on a huge experience with this disease and are, therefore, of great interest and value to any student of internal medicine. One would wish the authors had presented more case material and statistical analyses from their experiences to allow the reader to see how they had arrived at some of their conclusions. This data would have been desirable in the sections on "Mild Cases" and on "Bacteria-free Cases," both of which concepts are usually attributed to the senior of the two authors. They state that nearly all of their mild cases have recovered. This is a remarkable observation in a disease in which spontaneous recovery has always been thought to be rare. One would wish for more details about these interesting cases and further explanations of how they differ from the ordinary cases of this disease which almost never recover spontaneously. Many questions come to mind concerning the concept of the bacteria-free stage. The distinction between recovery and the bacteria-free stage is not a clear one. In the section on prognosis the authors stated that some patients adequately treated with antibiotics go on to die of heart failure or embolization despite the fact that their blood cultures had become negative during treatment. Are these examples of the bacteria-free stage? From the standpoint of analysis of antibiotic therapy it would be important to know whether these patients had recovered from the infection and were suffering from sequelae of the disease or whether they were in an active but bacterial-free stage.

This book, despite some of the questions it leaves unanswered, is a valuable monograph and should be read by all who are interested in subacute bacterial endocarditis.

THOMAS W. CLARK, M.D.

CARDIOPATIAS CONGENITAS DE LA INFANCIA. By Augustín Castellanos y Gonzalez. La Habana, 1948, M. V. Fresneda, 448 pages, 82 figures, and 20 plates. Price $9.00.

This book is devoted to the study of congenital heart diseases in children. The first part considers the embryology and the physical and technical examination of the heart. The second part discusses cyanosis and the signs of the "blue disease." The third part consists of a detailed study of the various clinical-anatomical syndromes.

Of special value to the cardiologist are the chapters dealing with (1) the development and anomalies of the large veins; (2) the classification of congenital heart diseases on the basis of cyanosis and murmurs; and (3) angiocardiography. The latter technique is studied first as a method; it is then demonstrated in its application to the various diseases and illustrated by excellent sketches. Actual angiocardiograms are presented at the end of the book.

It is to be noted that certain chapters, not based on original studies, are already old; for example, the chapter presenting phonocardiographic data obtained prior to 1937. Other chapters are too brief. It is to be regretted that the author fails to give his personal views on some of the more controversial issues. Several misprints of names somewhat mar the book. The bibliography is limited. A good index is placed at the end.

This book should be useful chiefly to students of angiocardiography, a technique largely developed in children through the widely known work of Castellanos and his School.

A. LUISADA, M.D.

DIRECT ELECTROCARDIOGRAPHY OF THE HUMAN HEART AND INTRATHORACIC ELECTROCARDIOGRAPHY. By Franz M. Groedel, M.D., and Paul R. Borchardt, M.D., F.C.C.P. New York, 1948, Brooklyn Medical Press, Inc., 224 pages, 38 tables, and 29 illustrations. Price $9.00.

The authors present in detail previously reported results of direct electrocardiographic explorations of the epicardial surfaces obtained from subjects undergoing pneumolysis or pneumonectomy. It is evident from the figures that the electrocardiographic patterns obtained by the authors from auricular and ventricular surfaces during normal activation and during extrasystoles confirm present electrocardiographic concepts. Comparative examinations obtained by simultaneously recording leads from the cardiac surfaces and from the precordium again demonstrate that chest leads may be taken as an adequate representation of cardiac segments subjacent to the exploring electrode. The presentation of this extensive material is of value to those concerned with supplanting empirical knowledge of electrocardiography by factual evidence on spread and distribution of action currents.

The mass of detailed information and an awkwardly written text somewhat obscure the results of relatively simple and valid experiments. The authors have attempted interpretations which are frequently at variance with established electrophysical facts, and the disregard of investigative work outside the orbit of the authors impairs the usefulness of an otherwise interesting monograph

HANS H. HECHT, M.D.

AN INTRODUCTION TO CARDIOLOGY. By Geoffrey Bourne, M.D., F.R.C.P. Baltimore, 1949, Williams and Wilkins Company, 264 pages and 65 figures. Price $4.50.

In the words of the author it is the purpose of this book to portray in successive chapters, the chief aspects of cardiovascular disease. The plan of presentation is good and the book is easily read. It contains several statements which may be questioned such as, "Left sided failure is usually the result of mitral stenosis . . . ." The discussion of digitalis and digitalis therapy is inadequate even for a book of this type. Too much space is given to certain subjects; for example, the thyroid gland and heart disease. The examination of the heart by x-ray studies is well presented and the illustrations on this subject are well chosen. The discussions on effort syndrome (neurocirculatory asthenia), left submammary pain, and prognosis in myocardial infarction are good. The book has been written for the busy practitioner and the medical student and holds little of interest or value for the internist or cardiologist.

JOSEPH B. VANDER VEER, M.D.

AN ATLAS OF ELECTROCARDIOGRAPHY. By William Dressler, M.D., and Hugo Roesler, M.D. Springfield, Illinois, 1949, Charles C Thomas, Publisher, 503 pages and 439 figures. Price $14.00.

This book, intended as an aid to those familiar with the fundamentals of electrocardiography, contains nearly 450 electrocardiographic illustrations of excellent technical quality, neatly mounted, and faithfully reproduced. On the facing pages are found the description of each curve, a concise objective diagnosis, the clinical data, and a final comment dealing with the practical application and proper understanding of the observed electrocardiographic changes.

The electrocardiograms illustrating changes from the normal both as to form or rhythm have not been grouped according to etiologic or pathologic conditions, but instead, those curves which display similar "patterns" are arranged together, a system which seems ideally suited to the study of differential diagnosis in an atlas presentation. The summaries which follow each of these groups supplement the atlas with an unusual amount of excellently prepared didactic material. The discussion accompanying the section on unipolar limb leads is particularly worthy of comment; it is a concise, lucid, and reasonable summary of the subject. The plan involves some repetition of material, particularly in regard to myocardial infarction, but on the other hand, often serves to emphasize different aspects.

Because of an unavoidable delay in the publication of the atlas two entire sections, "Advances in the Electrocardiographic Diagnosis of Myocardial Infarction" dealing largely with the newer application of multiple precordial leads, and "Interpretation of the Electrocardiogram with the Aid of Unipolar Limb Leads" were added in order to bring the finished book completely up to date. It is regrettable that this material, particularly that dealing with the unipolar limb leads, could not have been integrated with the presentations of such matters as axis deviation, Q deflections, myocardial infarction, and ventricular hypertrophy. In subsequent revisions it is hoped that this can be done.

The content is uniformly good. Occasionally the authors appear to accept the diagnosis of myocardial infarction rather too readily when the changes in the electrocardiograms are confined alone to the T waves, although usually only after the clinical data have been incorporated in the final interpretation. In the reviewer's opinion too much emphasis has been placed upon the "T_1 less than T_3" pattern as an index of infarction without pointing out that this results simply from the forces which produce a reduction in amplitude or inversion of the T wave in Lead aV_L, a situation present in most cases of anterior infarction or occasionally when the heart is in the vertical position. The section on the normal electrocardiogram could have been greatly strengthened by incorporating a number of records of infants and children taken with complete chest and unipolar limb leads, a subject of considerable general interest at present. These are, however, only minor criticisms of an excellent book.

The index is complete and well organized. It serves to bring together the various parts of a subject which, because of the plan of the book, appear in scattered sections.

Because it has not only the merits of an atlas presentation but also incorporates an unusual amount of teaching material, the book should receive wide acceptance in the study of electrocardiography.

E. M. KLINE, M.D.

RÖNTGENDIAGNOSTIK DES HERZENS UND DER GROSSEN GEFASSE, Second Edition. By Prof. Dr. Erich Zdansky. Vienna, 1949, Springer-Verlag, 434 pages, 5 tables, and 397 figures. Price $22.00.

This is the second edition of a comprehensive work on cardiovascular roentgenology. Revisions and additions are relatively few, undoubtedly attributable to the author's enforced exile just before and during the war years. An all too brief section of five pages is devoted to angiocardiography; no mention at all is made of electrokymography, a new and important tool available since 1945.

Revisions have occurred in the sections on heart size measurements, derived calculations of heart volume, and the effects of arteriovenous shunts on the heart. New sections include brief discussions on atrophy of the heart, hypertrophy and dilatation, and functional tests utilizing roentgenographic methods.

The portions of the book devoted to the individual chambers of the heart and to the great vessels are authoritative and well and profusely illustrated. This is gratifying for in the following eighty pages the author reverts to the typical configurations in various valvular and nonvalvular affections which have in the past misled both clinicians and roentgenologists. However, even here there is a wealth of data and detail which is worthwhile as a source for references.

Particularly interesting are the sections devoted to constrictive pericarditis, the lungs in chronic passive congestion, to cardiac displacement, and to the aorta in health and disease.

On the whole the book measures up well as a reference volume; it is too discursive and detailed for use as a text. The diagrams and half-tone reproductions are unusually good.

JOHN BERNARD SCHWEDEL, M.D.

CARDIAC CATHETERIZATION IN CONGENITAL HEART DISEASE. By Andre Cournand, M.D., Janet S. Baldwin, M.D., and Aaron Himmelstein, M.D. New York, 1949, The Commonwealth Fund, 108 pages and 17 illustrations. Price $4.00.

This book, as the authors state in their introduction, deals primarily with the noncyanotic malformations of the heart. It is divided into a general and a special part.

The general section deals with equipment, technique, and with complications of catheterization of the heart in general. This section is also concerned with a general discussion of the characteristic blood pressure tracings obtained and with the formulas used in calculating the various volume flows and shunts in congenital heart disease. Cournand and his co-workers who have done so much to initiate and standardize the technique of catheterization, describe the equipment which is used in their laboratory, i.e., the intravenous catheter, first described in 1941. The authors do not mention more recent types of catheters which permit more rapid sampling of blood. There is also no mention of the use of a stylette within the catheter which gives the tube additional rigidity and makes it easier to guide. The authors use a modified Hamilton manometer and also mention the more popular electric recording devices. Cournand and his co-workers perform catheterization in children under nine years of age under basal Avertin anesthesia. It should be mentioned, however, that in many instances the use of morphine-scopolamine is preferable. Air emboli, venous and intracardiac thrombosis, and cardiac arrythmias are mentioned as the more frequent complications of catheterization in congenital heart disease. Fortunately, all of these complications are so rare that the combined deaths from cardiac catheterization reported from various laboratories is probably less than 0.1 per cent. Cardiac arrythmias are undoubtedly the most frequent complications and the advice of the authors to use an electrocardiogram in conjunction with intracardiac catheterization is well given. The pressure recordings are excellent. The illustrations of characteristic tracings from the right and left auricle, right and left ventricle, the pulmonary artery, and the aorta should be of greatest value to all those who are interested in the diagnosis of congenital heart disease by physiological methods. Formulas for the calculation of the various volume flows and shunts are similar to those used by other workers in this field.

The second part of the book deals with specific malformations of the heart and great vessels. Of particular value is the correlation of clinical, roentgenological, and physiological findings. By detailed description of the findings in individual cases, the authors are able to establish patterns which exist in the more typical forms of congenital heart disease. Some of the more common malformations are subdivided according to differences in the hemodynamics (i.e., pulmonary artery pressure). This is of the greatest importance since it stresses the fact, which has been so often overlooked in the past, that a similarity in gross pathology is often associated with a great variety of physiological and therefore clinical findings.

The book represents a great contribution to a rapidly progressing branch of medicine and surgery. It should be considered essential by all those who plan to apply catheterization of the heart as a diagnostic tool in the study of congenital heart disease.

RICHARD J. BING, M.D.

CORONARY ARTERY DISEASE. By Ernst P. Boas, M.D., and Norman F. Boas, M.D. Chicago, Ill., 1949, The Year Book Publishers, Inc., 309 pages and 88 illustrations. Price $6.00.

Except for the therapeutic use of anticoagulants, comparatively little that is new has appeared during the past few years relating to the clinical aspects of coronary heart disease. In this com-

pact book, the Boases have given a good summary of current knowledge. The senior author for many years has been interested in this subject and has contributed to the literature concerning it. He is, therefore, in a position to express critical opinions concerning controversial matters. The arrangement of chapters has resulted in some unnecessary repetition. Coronary insufficiency is disposed of with relative brevity. Consideration of treatment is adequate and the use of various drugs is discussed in the light of their pharmacologic action according to the best evidence available. Westsal is recommended as a salt substitute although it has recently been condemned because of the toxic effects of lithium. Probably the book was in press before these unfortunate clinical experiences were published.

The chief criticism, in the opinion of this reviewer, is the lack of logical sequence in the presentation of the material. Arteriosclerosis is the main cause of coronary heart disease. Coronary insufficiency, occlusion, thrombosis, and cardiac infarction are episodes in the evolution of this process. Congestive heart failure is the result of the damage to the myocardium. This is a simple concept and upon an understanding of it, rests rational therapy.

An adequate bibliography of some 400 key references is given. The style is clear and the publishers have creditably performed their part. In the words of the authors, "the book is designed as a useful tool for the practicing physician, but the presentation is sufficiently detailed to make it of interest to the cardiologist as well."

ROBERT L. LEVY, M.D.

SHOCK AND ALLIED FORMS OF FAILURE OF THE CIRCULATION. By H. A. Davis, M.D., C.M., F.A.C.S. New York, 1949, Grune and Stratton, 595 pages, 55 figures, and 17 tables. Price $12.00.

The advances made in the definition and treatment of shock during recent years as well as the scattered studies which preceded the concentrated effort made in World War II have long been in need of, and at last been given, a unified presentation. So great has been the need that it is curious that books such as this do not abound. One reason is the diversity of opinion among potential authors, the need for a penetrating analysis of an extensive literature, and the fact that few have the ability or interest to compass all the phenomena incident to shock, recovery therefrom, and "allied forms of failure of the circulation."

This book opens with a historical review and proceeds through definitions to consider the pathogenesis of shock (physiological, biochemical, and histological), the special types of circulatory failure (adrenal, infectious, obstetric, burn, and anesthetic), and the treatment of each. In so doing, the author demonstrates his familiarity with the field, which he carefully documents. He does not pretend to a magisterial or dogmatic conclusiveness. Rather, he achieves an unusual and refreshing impartiality in the evaluation of the work of others. The objection may be raised that he seems at times to devote disproportionate space to his own observations. This is not a serious objection to the book as a whole. In common with most who have labored in this vineyard, we note also that (according to our lights) not enough is made of arterial transfusion, elective hypotension, and so on. But, in general, the treatment is comprehensive and exact.

Thus, what needed doing, has been done well. The technical makeup is satisfactory. The book can be recommended to all who have to deal with shock and injury, both experimentally and clinically.

I. H. PAGE, M.D., AND A. C. CORCORAN, M.D.

FUNDAMENTALS OF INTERNAL MEDICINE. By Wallace M. Yater, M.D. Third Edition. New York, 1949, D. Appleton-Century-Crofts Company, Inc., 1,451 pages and 315 figures.

The third edition of this popular text, retaining its original concept, covers the vast field of internal medicine with simplification, conciseness, and elimination of theoretical and redundant material. The first 190 pages of the volume outline the essential features of diseases of the heart and blood vessels and form the basis of this review.

Most of this section is again the work of the senior author. The discussion of the diagnosis and treatment of the various etiologic types of heart disease reflects his rich clinical experience. A new and enlarged article on electrocardiography by Dr. Joseph M. Barker brings this subject

up to date. In keeping with the goal of the textbook, a surprisingly large amount of information is contained here. Following a clear presentation of the fundamentals of a rapidly growing subject, the precordial leads are described and evaluated. The unipolar leads, including augmented unipolar extremity leads, are also discussed.

In the opinion of this reviewer, few textbooks of medicine contain as much new information on various aspects of the subject of cardiovascular disease as the present edition of Dr. Yater's *Fundamentals of Internal Medicine.*

WILLIAM G. LEAMAN, JR., M.D.

A PRIMER OF ELECTROCARDIOGRAPHY, Second Edition. By George E. Burch, M.D., and Travis Winsor, M.D. Philadelphia, 1949, Lea & Febiger, 245 pages, 265 illustrations, and 6 tables. Price $4.50.

This small volume continues to be, in the opinion of the reviewer, the bext textbook on electrocardiography now available because, as the authors state in the preface to this second edition, "Re-emphasized is the need for understanding the mechanisms by which electrocardiographic patterns are developed rather than memorizing the patterns and interpreting them empirically."

Except for a number of minor criticisms of no great practical importance, the first two chapters, outlining the fundamental principles upon which electrocardiographic diagnosis should be based, are excellent. As examples of the matters which troubled the reviewer, consider first the statement at the bottom of page 59, "*Overshooting* is produced by a loose string." This type of artifact is due, not to a loose string, but to a condenser-like action occurring beneath the electrodes and is rarely seen with the metal plates, properly applied with electrode paste, now in general use. A string that is too loose is usually over-damped and cannot respond to quick deflections, which may be greatly decreased in size or disappear entirely. Again on page 87 in the section headed *Right Axis Deviation*, it is stated that, "such disease states as . . . . interventricular septal defect, patent ductus arteriosus, ... are commonly associated with the electrocardiographic picture of *right axis deviation*." This is not true of these two conditions. As a matter of fact, on pages 193 and 194 in Chapter V, it is made clear that right axis deviation does not occur with a simple patent ductus arteriosus. The reviewer has always considered the use of the terms right and left ventricular strain as electrocardiographic double talk and is sorry to see them used so freely in this volume.

The expanded chapter on precordial leads which includes a fairly extensive discussion of the unipolar extremity leads is excellent as are the final chapters on the cardiac arrhythmias and clinical applications of the electrocardiogram. The latter section includes a fairly detailed and entirely lucid discussion of the ventricular gradient.

Finally, the statements at the end of the volume pointing out the limitations of usefulness of electrocardiograms and urging conservatism in their interpretation must be applauded.

F. D. JOHNSTON, M.D.

Acknowledgement of Books Received but not Reviewed

COLLATERAL CIRCULATION (ANATOMICAL ASPECTS) By Daniel P. Quiring, Ph.D., Head of the Anatomy Division, Cleveland Clinic Foundation, and Associate Professor of Biology, Western Reserve University. Philadelphia, 1949, Lea & Febiger, 142 pages. Price $5.00.

CLINICAL CASE-TAKING. GUIDES FOR THE STUDY OF PATIENTS. HISTORY-TAKING AND PHYSICAL EXAMINATION OR SEMIOLOGY OF DISEASE IN THE VARIOUS SYSTEMS, Fourth Edition. By George R. Herrmann, M.D., Ph.D., Professor of Medicine, University of Texas. St. Louis, 1949, The C. V. Mosby Company, 240 pages.

ON MYOGLOBIN AND ITS OCCURRENCE IN MAN. By Gunnar Biorck. From the Biochemical Department of the Medical Nobel Institute, The Cardiac Clinic of Sodersjukhuset, and the Department of Pathology at Sodersjukhuset, Stockholm, Sweden. Stockholm, Sweden, 1949, Supplement CCXXVI (226), Acta Medica Scandinavica, 216 pages.

SOME SUPPLEMENTARY LEADS IN CLINICAL ELECTROCARDIOGRAPHY. By Karl Erik Grewin. Stockholm, Sweden, 1948, Ivar Haeggstroms Boktryckeri A. B., 463 pages, 142 figures and 50 tables.

American Heart Association, Inc.

1775 Broadway, New York 19, N. Y.

Telephone Plaza 7-2045

ANNUAL MEETING

The Annual Meeting and Twenty-Third Scientific Session of the American Heart Association will be held at the Fairmont Hotel, San Francisco, June 22-25, 1950. All those desiring to attend should make room reservations at the earliest possible date.

PROGRAM COMMITTEE

The Chairman of the Program Committee for the Annual Scientific Session is Doctor Louis E. Martin, 1136 West Sixth Street, Los Angeles 14, California. All who desire to present papers at the meetings in San Francisco should forward to Doctor Martin an abstract (in triplicate) of the proposed presentation of not more than 300 words. The deadline for the receipt of abstracts is March 1, 1950.

Louis E. Martin, M.D., Chairman
1136 West Sixth Street
Los Angeles 14, Calif.

Graham Asher, M.D.
1220 Professional Bldg.
Kansas City, Mo.

Walter Bauer, M.D.
Massachusetts General Hospital
Boston, Mass.

Robert H. Bayley, M.D.
Oklahoma University
School of Medicine
Oklahoma City, Okla.

Richard J. Bing, M.D.
Johns Hopkins Hospital
Baltimore, Md.

Meyer Friedman, M.D.
Mount Zion Hospital
2200 Post Street
San Francisco, Calif.

William Goldring, M.D.
1088 Park Avenue
New York, N. Y.

Robert E. Gross, M.D.
Children's Hospital
330 Longwood Avenue
Boston, Mass.

Hans Hecht, M.D.
University of Utah Medical School
Salt Lake City, Utah

William P. Holbrook, M.D.
2430 E. Sixth Street
Tucson, Arizona

Franklin D. Johnston, M.D.
P. O. Box 276
Ann Arbor, Mich.

Hugh McCulloch, M.D.
La Rabida Sanitarium
Chicago, Ill.

Johnson McGuire, M.D.
2583 Grandin Rd.
Cincinnati, Ohio

Edgar M. McPeak, M.D.
4705 Montrose Blvd.
Houston, Texas

Ernest W. Page, M.D.
University of California
Medical School
San Francisco 22, Calif.

William Paul Thompson, M.D.
1930 Wilshire Blvd.
Los Angeles, Calif.

Irvine H. Page, M.D.
Cleveland Clinic
Euclid Avenue and 93rd Street
Cleveland, Ohio

Harry E. Ungerleider, M.D.
393 Seventh Avenue
New York, N. Y.

Helen B. Taussig, M.D.
Johns Hopkins Hospital
Medical School
Baltimore, Md.

Paul D. White, M.D.
264 Beacon Street
Boston, Mass.

CASES SOLICITED FOR REGISTRY OF CARDIOVASCULAR PATHOLOGY

Contribution of cases is being currently solicited for the Registry of Cardiovascular Pathology which has been set up, under the Association's sponsorship, in the American Registry of Pathology at the Armed Forces Institute of Pathology in Washington, D. C. Wallace M. Yater, M.D., is Chairman of the Registry Committee and its other members are Jesse E. Edwards, M.D.; Jane S. Robb, M.D.; Joseph T. Roberts, M.D.; and Helen B. Taussig, M.D. Communications regarding the registry should be addressed to The Director, Armed Forces Institute of Pathology, Washington 25, D. C.

The scope of the Registry is outlined as: a) congenital anomalies of the heart and larger blood vessels; b) subacute bacterial endocarditis; c) the so-called "diseases of the Collagen System" including polyarteritis nodosa, temporal arteritis, disseminated lupus erythematosus, Libman-Sacks endocarditis, scleroderma, and amyloidosis of the heart; d) primary tumors of the heart, pericardium, blood vessels and lymphatics, including rhabdomyomatosis and glycogen-storage disease.

In addition, cases illustrating other diseases of the heart and larger blood vessels, in which consultation is desired or which are of especial interest because of rarity or noteworthy clinico-pathologic correlation will be considered.

1950 RESEARCH GRANTS AND FELLOWSHIPS OF THE LIFE INSURANCE MEDICAL RESEARCH FUND

Applications for 1950 grants-in-aid of research on cardiovascular problems will be received by the Life Insurance Medical Research Fund up to January 1, 1950. Support is available for physiological, biochemical, and pathological research which bears on cardiovascular problems, as well as for clinical investigation in this field. Preference is given to fundamental research. It is expected that about $550,000 will be awarded for these grants.

Applications for postgraduate fellowships for training in research in 1950-51 will also be received by this Fund up to January 1, 1950. Preference is given to candidates wishing to work in the broad field of cardiovascular function or disease and to candidates wishing to work in institutions other than those in which they have obtained most of their experience. A doctor's degree (M.D. or Ph.D.), or the equivalent, is required. The annual stipend varies, as a rule being between $3,000 and $4,000, with larger amounts in special cases. At least 12 postgraduate fellowships will be available.

New grants and fellowships will become available on July 1, 1950.

Further information and application blanks may be secured from the Scientific Director, Life Insurance Medical Research Fund, 2 East 103rd Street, New York 29, N. Y. A number of pre-doctoral fellowships for basic training in research will also be awarded. Details are available upon request.

INDEX TO VOLUME 38

AUTHORS INDEX*

A

ABELL, LIESE LEWIS. (*See* Davidson, Abell, and Kendall (Proc.), 462*

ACKERMAN, A. J. (*See* Moyer and Ackerman), 799*

ADOLPH, WILLIAM. (*See* Lack, Adolph, Ralston, Leiby, Winsor, and Griffith), 654

AGRESS, CLARENCE M. (*See* Rosenburg and Agress), 593

AHN, BERTIL v., AND GÖHLE, OLLE. A case of angina pectoris precipitated chiefly by tobacco smoking and meals, 775

AKMAN, L. (*See* Stamler, Bolene, Katz, Harris, Silber, Miller, and Akman) (Proc.), 466*

ALFIN-SLATER, R. (*See* Deuel, Marx, Alfin-Slater, and Marx) (Proc.), 463*

ALLEN, A. W., AND DONALDSON, G. A. Venous thrombosis and pulmonary embolism, 639*

ALLEN, E. V. (*See* Morgan, Allen, and MacCarty), 444*

ALTO, P. (*See* Thomas, Alto, and Garland), 311*

ALTSCHUL, RUDOLF. Histology of infarcted heart muscle (Proc.), 473*

ALTSHULER, S. S., HOFFMAN, K. M., AND FITZGERALD, P. J. Electrocardiographic changes in diphtheria, 137*

AMROMIN, G. D., SCHLICHTER, J. G., AND SOLWAY, A. J. L. Medionecrosis of the aorta, 639*

ANGLE, R. G. (*See* Ferraro and Angle), 315*

APPERLY, F. L., AND CARY, M. K. The control of circulatory stasis by the electrical stimulation of large muscle groups, 448*

ARATA, JUSTIN E. (*See* Weinstein and Arata), 781

ASHWORTH, C. T., AND HAYNES, D. M. Lesions in elastic arteries associated with hypertension, 310*

ASSALI, N. S. (*See* Brust, Assali, and Ferris), 927*

ATTYAH, A. M. (*See* Hamilton, Riley, Attyah, Cournand, Fowell, Himmelstein, Noble, Remington, Richards, Jr., Wheeler, and Witham), 314*

B

BAGEANT, W. E., AND RAPEE, L. A. The treatment of pulmonary embolus by stellate block, 151*

BAHNSON, HENRY T., COOLEY, ROBERT N., AND SLOAN, ROBERT D. Coarctation of the aorta at unusual sites, 905

BAKER, ROGER D., AND KENT, SIDNEY P. Nature of the hyaline material in arteriolosclerosis of kidney (Proc.), 470*

BALDWIN, DAVID. (*See* Taylor, Baldwin, and Haas) (Proc.), 464*

BALKIN, S. S., AND GOOTNICK, A. The effects of Dicumarol on the electrocardiogram, 145*

BARKER, JOSEPH M., AND VALENCIA, FERNANDO. The precordial electrocardiogram in incomplete right bundle branch block, 376

BARKER, N. W. (*See* Parker and Barker), 636*

BARNES, C. G., FATTI, L., AND PRYCE, D. M. Arteriovenous aneurysm of the lung, 446*

BARNES, D. W. H., LOUTIT, J. F., AND REEVE, E. B. A comparison of estimates of circulating red blood cell volume given by the Ashby marked red cell method and T 1824 hematocrit method in man, 630*

——, ——, AND ——. Observations on the estimate of the circulating red blood cell volume in man given by T 1824 and the hematocrit, with special reference to uncorrected dye loss from the circulation, 631*

BATTERMAN, R. C. (*See* DeGraff, Batterman, and Rose), 626*

BAYGIN, R. (*See* Soulie, Michel, and Baygin), 632*

BEAN, D. M. (*See* Kergin, Bean, and Paul), 628*

BECHGAARD, P. Paroxysmal ventricular fibrillation with recovery, 308*

BECK, C. S. Revascularization of the heart, 624*

BECKER, G. H. (*See* Necheles, Meyer, and Becker) (Proc.), 472*

BEEBE, RICHARD T., AND MENEELY, JOHN K., JR. *Brucella melitensis* endocarditis, 788

BEHRMANN, V. G. (*See* McClure, Behrmann, and Hartman), 623*

BELL, G. H. (*See* Lazarus, Munro, and Bell), 309*

BENJAMIN, ZACHARY H. Duration of the Q-T interval in normal pregnant women, 119

BENNETT, I. L., JR., AND HYEMAN, A. Paroxysmal hypertension associated with tabes dorsalis, 797*

BENNETT, W. A. (*See* Cluxton, Jr., Bennett, and Kepler), 452*

*An asterisk (*) after a page number indicates the reference is an abstract and not an original article.

BERENSON, G. Value of routine fluorograms as a measure for detecting cardiac abnormalities, 798*

BERG, BRUCE M. (*See* Hein and Berg), 433

BERG., W., DELIUS, L., AND SCHILDGE, E. Hypnosis and venous pressure, 309*

BERGMAN, H. C. (*See* Prinzmetal, Corday, Bergman, Schwartz, and Spritzler), 445*

——. (*See* Simkin, Bergman, Silver, and Prinzmetal), 310*

BERLIN, PERLA. (*See* Morrison, Berlin, and Gonzalez) (Proc.), 477*

——. (*See* Morrison, Chaney, Gonzalez, and Berlin) (Proc.), 477*

BERRETA, J. A. (*See* Etala and Berreta), 313*

BETTMAN, R. B., AND TANNENBAUM, W. J. Herniation of the heart, 925*

BEVANS, MARGARET, DAVIDSON, JACK D., AND KENDALL, FORREST E. The pathology of early lesions in experimental canine arteriosclerosis (Proc.), 462*

——. (*See* Steiner, Kendall, and Bevans), 34

BINE, R., JR., AND FRIEDMAN, M. Observations concerning the effects of blood upon the action of a digitalis glycoside, 796*

BING, R. J., HAMMOND, M. M., HANDELSMAN, J. C., POWERS, S. R., SPENCER, F. C., ECKENHOFF, J. E., GOODALE, W. T., HAFKENSCHIEL, J. H., AND KETY, S. S. The measurement of coronary blood flow, oxygen consumption, and efficiency of the left ventricle in man, 1

——. HANDELSMAN, J. C., CAMPBELL, J. A., GRISWOLD, H. E., AND BLALOCK, A. The surgical treatment and physiopathology of coarctation of the aorta, 623*

BJÖRKENHEIM, G. (*See* Frisk, Hammarström, Lagerlof, Werkö, Björkenheim, Holmgren, and Larsson), 934*

BLACK, BOYD K. (*See* Hicks and Black), 528

BLACKMAN, N. S., AND HAMILTON, C. I., JR. Serial electrocardiographic changes in young adults with acute rheumatic fever, 152*

BLACK-SCHAFFER, BERNARD. (*See* Race and BLACK-SCHAFFER), 501

BLALOCK, A. (*See* Bing, Handelsman, Campbell, Griswold, and Blalock), 623*

——. Surgical procedures employed and anatomical variations encountered in the treatment of congenital pulmonic stenosis, 793*

BLAND, E. F. (*See* Wang, Bland, and White), 451*

BLOOD, D. W., AND PATTERSON, M. C. Effect of aminophyllin on the coagulation of human blood, 628*

BLOOMFIELD, R. A., RAPOPORT, B., MILNOR, J. P., LONG, W. K., MEBANE, J. G., AND ELLIS, L. B. The effects of the cardiac glycosides upon the dynamics of the circulation in congestive heart failure, 156*

BOLENE, C. (*See* Katz, Horlick, Rodbard, Stamler, and Bolene) (Proc.), 465*

——. (*See* Stamler, Bolene, Katz, Harris, Silver, Miller, and Akman) (Proc.), 466*

BOLLMAN, J. L. (*See* Salassa, Bollman, and Dry), 929*

BOOKMAN, J. J. (*See* Megibow, Pollack, Megibow, Bookman, and Osserman) (Proc.), 468*

BOWLEY, C. C. (*See* Mowbray and Bowley), 146*

BOYD, E. J., AND WARNER, E. D. Effect of vitamin K on Dicumarol-induced hypoprothrombinemia in rats, 930*

BRADFIELD, JAMES Y., JR. (*See* Hejtmancik, Bradfield, Jr., and Miller), 757

BRIGGS, A. P., FOWELL, D. M., HAMILTON, W. F., REMINGTON, J. W., WHEELER, N. C., AND WINSLOW, J. A. Renal and circulatory factors in the edema formation of congestive heart failure, 928*

BRONSTEIN, J. The P wave in precordial leads in chronic bronchopulmonary disease, 312*

BROWN, F. (*See* Rodbard, Brown, and Katz), 863

BROWN, G. E., CLAGETT, O. T., BURCHELL, H. B., AND WOOD, E. H. Preoperative and postoperative studies of intraradial and intrafemoral pressures in patients with coarctation of the aorta, 634*

BROWN, HELEN BENNETT, AND PAGE, IRVINE H. The effect of graded dosages of iodide on plasma and liver cholesterol of normal, cholesterol-fed and thyroidectomized rabbits (Proc.), 479*

BROZEK, J., CHAPMAN, C. B., AND KEYS, A. Drastic food restriction: effect on cardiovascular dynamics in normotensive and hypertensive conditions, 140*

BROZEK, JOSEF. (*See* Simonson, Brozek, and Keys), 407

BRUST, A. A., ASSALI, N. S., AND FERRIS, E. B. The evaluation of neurogenic and humoral factors in blood pressure maintenance in normal and toxemic pregnancy using tetraethylammonium chloride, 927*

BURCH, GEORGE E. (*See* Conway, Cronvich, and Burch), 537

BURCHELL, H. B. An evaluation of esophageal electrocardiograms in the diagnosis of healed posterior myocardial infarction, 794*

——. (*See* Brown, Clagett, Burchell, and Wood), 634*

BURCHELL, HOWARD B. (*See* Edwards, Douglas, Burchell, and Christensen), 205

BURFORD, T. H. (*See* Carson, Burford, Scott, and Goodfriend), 930*

BURNS, R. A., JR., JASPER, W. H., AND WAKERLIN, G. E. The effect of crude renal extracts and purified renin on vascular lesions in experimental malignant renal hypertension (Proc.), 478*

C

CAHILL, G. F. Pheochromocytomas, 154*
CAMPBELL, D. A. (*See* Smith and Campbell), 793*
CAMPBELL, J. A. (*See* Bing, Handelsman, Campbell, Griswold, and Blalock), 623*
CARSON, M. J., BURFORD, T. H., SCOTT, W. G., AND GOODFRIEND, J. Diagnosis of pulmonary stenosis by angiocardiography, 930*
CARTER, R. A. (*See* Thorner, Carter, and Griffith), 641
CARY, M. K. (*See* Apperly and Cary), 448*
CHANEY, ALBERT L. (*See* Morrison, Chaney, Gonzalez, and Berlin) (Proc.), 477*
CHAPMAN, C. B. (*See* Brozek, Chapman, and Keys), 140*
CHRISTENSEN, N. A. (*See* Edwards, Christensen, Clagett, and McDonald), 633*
CHRISTENSEN, NORMAN A. (*See* Edwards, Douglas, Burchell, and Christensen), 205
CLAGETT, O. T. (*See* Brown, Clagett, Burchell, and Wood), 634*
——. (*See* Edwards, Christensen, Clagett, and McDonald), 633*
——. (*See* Wakim, Slaughter, and Clagett), 634*
——. The surgical treatment of coarctation of the aorta, 634*
CLARK, THOMAS E. (*See* Mahanna, Clark, and Kissane), 301
CLUXTON, H. E., JR., BENNETT, W. A., AND KEPLER, E. J. Anterior pituitary insufficiency (panhypopituitarism-Simmonds' disease), pituitary myxedema and congestive heart failure (myxedema heart); report of a case and findings at necropsy, 452*
COHEN, H., AND HARRISON, C. V. Temporal arteritis, 143*
CONCHA, J. B. (*See* Gunther and Concha), 933*
CONWAY, JOHN P., CRONVICH, JAMES A., AND BURCH, GEORGE E. Observations on the spatial vectorcardiogram in man, 537
COOLEY, ROBERT N. (*See* Bahnson, Cooley, and Sloan), 905
CORCORAN, A. C., MASSON, GEORGES, HAZARD, BEECH, AND PAGE, IRVINE H. Vascular lesions in experimental hypertension (Proc.), 464*
——. (*See* Masson, Glasser, Savard, Corcoran, and Page) (Proc.), 479*
CORDAY, E. (*See* Prinzmental, Corday, Bergman, Schwartz, and Spritzler), 445*
CORRELL, JAMES W. (*See* Kellner, Correll, and Ladd) (Proc.), 460*
COSBY, RICHARD S., AND GRIFFITH, GEORGE C. Interatrial septal defect, 80
COTTRALL, G. E. (*See* Paterson and Cottrall) (Proc.), 466*
COURNAND, A. (*See* Hamilton, Riley, Attyah, Cournand, Fowell, Himmelstein, Noble, Remington, Richards, Jr., Wheeler, and Witham), 314*
COURTER, S. R., FELSON, B., AND MCGUIRE, J. Familial interauricular septal defect with mitral stenosis (Lutembacher's syndrome), 795*
CRAGAN, M. D. (*See* Dolgopol and Cragan), 637*
CRONVICH, JAMES A. (*See* Conway, Cronvich, and Burch), 537
CUSICK, G. (*See* Green, Johnson, Lobb, and Cusick), 136*

D

DALE, ANTHONY D. (*See* Wolffe, Digilio, Dale, McGinnis, Donnelly, Plungian, Sprowls, James, Einhorn, and Werkheiser) (Proc.), 457*
D'ALTON, C. J., DARLING, R. C., AND SHEA, E. The insensible loss of water in congestive heart failure, 795*
DARLING, R. C. (*See* D'Alton, Darling, and Shea), 795*
DAUBER, D., HORLICK, L., AND KATZ, L. N. The role of desiccated thyroid and potassium iodide in the cholesterol-induced atherosclerosis of the chicken, 25
DAVIDSON, JACK D., ABELL, LIESE LEWIS, AND KENDALL, FORREST E. Serum lipids in experimental canine arteriosclerosis (Proc.), 462*
——. (*See* Bevans, Davidson, and Kendall) (Proc.), 462*
——. (*See* Kendall, Meyer, and Davidson) (Proc.), 474*
DAVIS, W. M. (*See* Herring and Davis), 925*
DAYRIT, C. (*See* Gold, Modell, Kwit, Shane, Dayrit, Kramer, Zahm, and Otto), 307*
DEGRAFF, A. C., BATTERMAN, R. C., AND ROSE, O. A. Digitoxin: its evaluation for initial digitalization of the patient with congestive heart failure, 626*
DELIUS, L. (*See* Berg, Delius, and Schildge), 309*
DEMUTH, W. E., AND RAWSON, A. J. Pseudomonas septicemia and endocarditis, 137*
DENST, JOHN. (*See* Swan, Trapnell, and Denst), 914
DE PALMA, A. F. Scalenus anticus syndrome treated by surgery and skeletal traction, 150*
DE TAKATS, G., JULIAN, O. C., AND FOWLER, E. F. The surgical treatment of essential hypertension. IV. Case selection and technique as influencing results, 638*
——. See also under T
DETERLING, RALPH A., JR., AND ESSEX, HIRAM E. Studies on peripheral circulation and epinephrine sensitization following sympathectomy, 248
DEUEL, H. J., JR., MARX, W., ALFIN-SLATER, R., AND MARX, L. The relationship of blood and liver cholesterol to atherosclerosis in different species (Proc.), 463*
DEXTER, L. (*See* Hellems, Haynes, Dexter, and Kinney), 449*

DIGILIO, VICTOR A. (*See* Wolffe, Digilio, Dale, McGinnis, Donnelly, Plungian, Sprowls, James, Einhorn, and Werkheiser) (Proc.), 467*
DOFF, SIMON D. (*See* Roth and Doff), 614
DOLGOPOL, V. B., AND CRAGAN, M. D. Myocardial changes in poliomyelitis, 637*
DONALDSON, G. A. (*See* Allen and Donaldson), 639*
DONEGAN, CHARLES K. (*See* Messer, Donegan, and Orgain), 732
DONNELLY, DANIEL J. (*See* Wolffe, Digilio, Dale, McGinnis, Donnelly, Plungian, Sprowls, James, Einhorn, and Werkheiser (Proc.), 467*
DONOVAN, G. E. Modern phonocardiography, 307*
DORSET, V. J., SPICKNALL, CHARLES G., AND TERRY, LUTHER L. Penicillin therapy of gonococcic endocarditis, 610
DOUGLAS, JOHN M. (*See* Edwards, Douglas, Burchell, and Christensen), 205
DOUGLASS, R. Anomalous pulmonary vessels, 628*
DRAKE, W. L., JR. (*See* Massey and Drake), 797*
DRY, T. J. (*See* Salassa, Bollman, and Dry), 929*
DUFF, G. L. (*See* McMillan and Duff), 635*
DUFF, G. LYMAN, AND PAYNE, TORRENCE, P. B. Studies on the mechanism of the inhibition of experimental cholesterol atherosclerosis in alloxan diabetes in the rabbit (Proc.), 460*
DURANT, THOMAS M., OPPENHEIMER, M. J., WEBSTER, M. R., AND LONG, JOAN. Arterial air embolism, 481

E

ECKENHOFF, J. E. (*See* Bing, Hammond, Handelsman, Powers, Spencer, Eckenhoff, Goodale, Hafkenschiel, and Kety), 1
ECKERSTROM, A. Libman-Sacks syndrome, 309*
EDMONDS, D. G. (*See* Wright, Osborn, and Edmonds), 932*
EDWARDS, E. A. Nail changes in functional and organic arterial disease, 443*
EDWARDS, J. E., CHRISTENSEN, N. A., CLAGETT, O. T., AND MCDONALD, J. R. Pathologic considerations in coarctation of the aorta, 633*
——. (*See* White and Edwards), 632*
EDWARDS, JESSE E., DOUGLAS, JOHN M., BURCHELL, HOWARD B., AND CHRISTENSEN, NORMAN A. Pathology of the intrapulmonary arteries and arterioles in coarctation of the aorta associated with patent ductus arteriosus, 205
EFFERSØE, P. Nephrectomy in hypertension and unilateral renal disorder, 629*
EICHNA, L. W. Thermal gradients during varying body temperatures, 925*
EILERT, MARY LOU. The effect of estrogens upon the partition of the serum lipids in female patients (Proc.), 472*
EINHORN, CLAIRE. (*See* Wolffe, Digilio, Dale, McGinnis, Donnelly, Plungian, Sprowls, James, Einhorn, and Werkheiser) (Proc.), 467*
ELKINS, E. C. (*See* Wakim, Gersten, Herrick, Elkins, and Krusen), 153*
ELLIOTT, K. A. C. (*See* Rabinovitch, Elliott, and McEachern), 135*
ELLIS, L. B. (*See* Bloomfield, Rapoport, Milnor, Long, Mebane, and Ellis), 155*
——. (*See* Harken, Ellis, Ware, and Norman), 932*
ERF, L. A., FOLDES, J., PICCIONE, F. V., AND WAGNER, F. B., JR. Pulmonary hemangioma with pulmonary artery-aortic septal defect, 766
ERNSTENE, A. CARLTON, AND PROUDFIT, WILLIAM L. Differentiation of the changes in the Q-T interval in hypocalcemia and hypopotassemia, 260
ESSEX, HIRAM E. (*See* Deterling, Jr., and Essex), 248
ESTES, J. EARLE. The prognosis in abdominal aortic aneurysm (Proc.), 470*
ETALA, F., AND BERRETA, J. A. A clinical and anatomical study of the post-tachycardia syndrome, 313*
EVANS, J. A. (*See* Jones, Younghusband, and Evans), 792*
EVANS, L. R., AND WHITE, P. D. Massive hypertrophy of the heart with special reference to Bernheim's syndrome, 794*

F

FARBER, EUGENE M. (*See* Hines, Jr., Farber, and Keith) (Proc.), 468*
FATTI, L. (*See* Barnes, Fatti, and Pryce), 446*
FELSON, B. (*See* Courter, Felson, and McGuire), 795*
FERRARO, L. R., AND ANGLE, R. G. Pheochromocytoma with symptoms of epinephrine shock, 315*
FERRIS, E. B. (*See* Brust, Assali, and Ferris), 927*
——. (*See* Stead, Reiser, Rapoport, and Ferris), 928*
FETTERMAN, G. H. (*See* Menten and Fetterman), 448*
FITZGERALD, P. J. (*See* Altshuler, Hoffman, and Fitzgerald), 137*
FLAUM, GERALD, AND THOMAS, EVAN W. Penicillin therapy of cardiovascular syphilis, 361
FLAXMAN, N. Digitoxin poisoning, 137*
FLEISCHNER, F. G. (*See* Luisada and Fleischner), 308*
FOLDES, J. (*See* Erf, Foldes, Piccione, and Wagner, Jr.), 766
FOLK, B. P., ZIERLER, K. L., AND LILIENTHAL, J. L., JR. Distribution of potassium and sodium between serum and certain extracellular fluids in man, 315*
FOWELL, D. M. (*See* Briggs, Fowell, Hamilton, Remington, Wheeler, and Winslow), 928*

FOWELL, D. M. (*See* Hamilton, Riley, Attyah, Cournand, Fowell, Himmelstein, Noble, Remington, Richards, Jr., Wheeler, and Witham), 314*
FOWLER, E. F. (*See* De Takats, Julian, and Fowler), 638*
FOWLER, EDSON F. (*See* De Takats and Fowler), 234
FRANKEL, LEONARD. (*See* Goodman, Wasserman, Marcus, and Frankel) (Proc.), 475*
FRANKLAND, A. W. Embolism after penicillin-oil-beeswax, 143*
FREEDMAN, L. R. (*See* Mylon and Freedman), 509
FREEMAN, N. E., LEEDS, F. H., AND GARDNER, R. E. Arterectomy in the treatment of intractable pain following recovery from acute arterial occlusion, 329
FRIEDFELD, L., MARCUS, H. R., AND VORZIMER, J. J. Aminophyllin determination of circulation time, 443*
FRIEDLANDER, RICHARD D. (*See* Sokolow and Friedlander), 665
FRIEDMAN, C. L. (*See* Friedman, Friedman, and Polley), 313*
FRIEDMAN, M. (*See* Bine, Jr., and Friedman), 796*
FRIEDMAN, S. M., FRIEDMAN, C. L., AND POLLEY, J. R. Potentiation of the hypertensive effects of desoxycorticosterone acetate (DCA) - by various sodium salts, 313*
FRISK, A. R., HAMMARSTRÖM, S., LAGERLOF, H., WERKÖ, L., BJÖRKENHEIM, G., HOLMGREN, A., AND LARSSON, Y. Effect of tetraethylammonium in arterial hypertension, 934*

G

GARDNER, R. E. (*See* Freeman, Leeds, and Gardner), 329
GARLAND, L. H. (*See* Thomas, Alto, and Garland), 311*
GENTILE, C. A case of isolated congenital dextrocardia without inversion of the chambers and associated with left ventricular hypertrophy and anteroseptal myocardial infarction, 637*
GERBAUX, A. (*See* Lian and Gerbaux), 636*
GERSTEN, J. W. (*See* Wakim, Gersten, Herrick, Elkins, and Krusen), 153*
GIBSON, S. (*See* Potts, Gibson, and Rothwell), 635*
GLASSER, O. (*See* Masson, Glasser, Savard, Corcoran, and Page) (Proc.), 479*
GÖHLE, OLLE. (*See* Ahn and Göhle), 775
GOLD, H., MODELL, W., KWIT, N. J., SHANE, S. J., DAYRIT, C., KRAMER, M. L., ZAHM, W., AND OTTO, H. L. Comparison of ouabain with strophanthidin-3-acetate by intravenous injection in man, 307*
GOLDBERGER, EMANUEL. (*See* Pokress and Goldberger), 423
GOLDMAN, J., AND POLLAK, A. J. The hamster as experimental animal for the study of atheromatosis (Proc.), 474*
GOMEZ, G. E. Question of cardiac hypertrophy in residents of high altitudes, 139*
GONZALEZ, WILLIAM. (*See* Morrison, Chaney, Gonzalez, and Berlin) (Proc.), 477*
GONZALEZ, WILLIAM F. (*See* Morrison and Gonzalez) (Proc.), 471*
——. (*See* Morrison, Berlin, and Gonzalez) (Proc.), 477*
——. (*See* Morrison, Hall, and Gonzalez) (Proc.), 478*
GOODALE, W. T. (*See* Bing, Hammond, Handelsman, Powers, Spencer, Eckenhoff, Goodale, Hafkenschiel, and Kety), 1
GOODFRIEND, J. (*See* Carson, Burford, Scott, and Goodfriend), 930*
GOODMAN, E. N. (*See* White, Heroy, and Goodman), 138*
GOODMAN, JOSEPH I., WASSERMAN, SIGMUND, MARCUS, LOUIS J., AND FRANKEL, LEONARD. A study of atherosclerosis in diabetes mellitus (Proc.), 475*
GOOTNICK, A. (*See* Balkin and Gootnick), 145*
GORDIN, R. Alternating nodal and sinus rhythm in a case of situs viscerum inversus, 631*
GOVER, M. Variation of blood pressure and heart disease with age, and the correlation of blood pressure with height and weight, 148*
GREEN, A. A. (*See* Rapport, Green, and Page), 445*
GREEN, D. M., JOHNSON, A. D., LOBB, A., AND CUSICK, G. The effects of adrenalin in normal and hypertensive patients in relation to the mechanism of sustained pressure elevations, 136*
GREEN, R. S., IGLAUER, A., AND MCGUIRE, J. Alterations of radial or brachial intra-arterial blood pressure and of the electrocardiogram induced by tilting, 144*
GRIFFITH, GEORGE. (*See* Lack, Adolph, Ralston, Leiby, Winsor, and Griffith), 654
GRIFFITH, GEORGE C. (*See* Cosby and Griffith), 80
——. (*See* Thorner, Carter, and Griffith), 641
GRISWOLD, DWIGHT, AND KEATING, JOHN H., JR. Cardiac dysfunction in hyperthyroidism, 813
GRISWOLD, H. E. (*See* Bing, Handelsman, Campbell, Griswold, and Blalock), 623*
GROSS, JEROME. The biology of arterial tissue (Proc.), 461*
GROSSI, L., AND SEITUM, F. Acquired coarctation of the aorta near the diaphragm, 792*
GROSSMAN, M. (*See* Schlichter, Wilburne, and Grossman), 796*
GRUENWALD, PETER. Necrosis in the coronary arteries of newborn infants, 889
GUNDERSON, S. M. (*See* Palmer and Gunderson), 933*
GUNTHER, B. S., AND CONCHA, J. B. A new method for the electrical recording of mechanical deformations, 933*

H

HAAS, GEORGE M. (*See* Taylor, Baldwin, and Haas) (Proc.), 464*

HAFKENSCHIEL, J. H. (*See* Bing, Hammond, Handelsman, Powers, Spencer, Eckenhoff, Goodale, Hafkenschiel, and Kety), 1

HALL, LILLIAN. (*See* Morrison, Hall, and Gonzalez) (Proc.), 478*

HALPERN, L. (*See* de Vries and Halpern), 295

HAMILTON, C. I., JR. (*See* Blackman and Hamilton), 152*

HAMILTON, W. F., AND REMINGTON, J. W. Some factors in the regulations of the stroke volume, 313*

——, RILEY, R. L., ATTYAH, A. M., COURNAND, A., FOWELL, D. M., HIMMELSTEIN, A., NOBLE, R. P., REMINGTON, J. W., RICHARDS, D. W., JR., WHEELER, N. C., AND WITHAM, A. C. Comparison of the Fick and dye injection methods of measuring the cardiac output in man, 314*

——. (*See* Briggs, Fowell, Hamilton, Remington, Wheeler, and Winslow), 928*

HAMMARSTRÖM, S. (*See* Frisk, Hammarström, Lagerlof, Werkö, Björkenheim, Holmgren, and Larsson), 934*

HAMMOND, M. M. (*See* Bing, Hammond, Handelsman, Powers, Spencer, Eckenhoff, Goodale, Hafkenschiel, and Kety), 1

HANDELSMAN, J. C. (*See* Bing, Hammond, Handelsman, Powers, Spencer, Eckenhoff, Goodale, Hafkenschiel, and Kety), 1

——. (*See* Bing, Handelsman, Campbell, Griswold, and Blalock), 623*

HARKEN, D. E., ELLIS, L. B., WARE, P. F., AND NORMAN, L. R. The surgical treatment of mitral stenosis. Valvuloplasty, 932*

HARRELL, G. T. (*See* Meads, Long, Pace, and Harrell), 926*

HARRIS, R. (*See* Stamler, Bolene, Katz, Harris, Silber, Miller, and Akman) (Proc.), 466*

HARRISON, C. V., AND LENOX, B. Heart block in osteitis deformans, 316*

——. (*See* Cohen and Harrison), 143*

HARTMAN, F. W. (*See* McClure, Behrmann, and Hartman), 623*

HAUPTMANN, A., AND MYERSON, A. Studies of finger capillaries in schizophrenia and manic-depressive psychoses, 145*

HAYNES, D. M. (*See* Ashworth and Haynes), 310*

HAYNES, F. W. (*See* Hellems, Haynes, Dexter, and Kinney), 449

HAZARD, BEECH. (*See* Corcoran, Masson, Hazard, and Page) (Proc.), 464*

HEIN, GORDON E., AND BERG, BRUCE M. Recovery from subacute bacterial endocarditis (*Streptococcus faecalis*), 433

HEJTMANCIK, MILTON R., BRADFIELD, JAMES Y., JR., AND MILLER, GEORGE V. Myocarditis and Friedreich's ataxia, 757

HELLEMS, H. K., HAYNES, F. W., DEXTER, L., AND KINNEY, T. D. Pulmonary capillary pressure in animals estimated by venous and arterial catheterization, 449*

HELMER, O. M. (*See* Shipley and Helmer), 314*

HEROY, W. W. (*See* White, Heroy, and Goodman), 138*

HERR, R. (*See* Meyer and Herr), 632*, 636*

HERRICK, J. F. (*See* Wakim, Gersten, Herrick, Elkins, and Krusen), 153*

HERRING, A. C., AND DAVIS, W. M. Penicillin treatment of subacute bacterial endocarditis, 925*

HIATT, E. P. Effects of repeated oral doses of quinine and quinidine on the blood pressure and renal circulation of dogs with experimental neurogenic hypertension, 449*

HICKAM, J. B. (*See* Myers and Hickam), 306*

HICKAM, JOHN B. Atrial septal defect. A study of intracardiac shunts, ventricular outputs, and pulmonary pressure gradient, 801

HICKS, SAMUEL P., AND BLACK, BOYD K. The relation of cardiovascular disease to apoplexy, 528

HIMMELSTEIN, A. (*See* Hamilton, Riley, Attyah, Cournand, Fowell, Himmelstein, Noble, Remington, Richards, Jr., Wheeler, and Witham), 314*

HINES, EDGAR A., JR., FARBER, EUGENE M., AND KEITH, NORMAN M. Changes in the cutaneous arterioles in the arm and leg in coarctation of the aorta (Proc.), 468*

HINES, L. E. (*See* Kessler and Hines), 627*

HIRATZKA, TOMIHARU. (*See* Myers, Klein, and Hiratzka), 547, 837

HOFF, H. E., AND STANSFIELD, H. Ventricular fibrillation induced by cold, 193

——. (*See* Nahum and Hoff), 798*

HOFFMAN, K. M. (*See* Altshuler, Hoffman, and Fitzgerald), 137*

HOFFMANN, C. R. (*See* Van Wyk and Hoffmann), 631*

HOLDEN, W. D. Aortic embolism, 925*

HOLMAN, RUSSELL L. Does arteriosclerosis develop by episodic stages? (Proc.), 469*

HOLMGREN, A. (*See* Frisk, Hammarström, Lagerlof, Werkö, Björkenheim, Holmgren, and Larsson), 934*

HOOBLER, SIBLEY W. (*See* Kert and Hoobler), 97

HORGER, E. L. (*See* Steward, Shepard, and Horger), 934*

HORLICK, L., AND KATZ, L. N. The relationship of atheromatosis development in the chicken to the amount of cholesterol added to the diet, 336

——, AND SURTSHIN, A. The role of anemia in the experimental production of heart block and auricular fibrillation in the dog, 716

——. (*See* Dauber, Horlick, and Katz), 25

——. (*See* Katz, Horlick, Rodbard, Stamler, and Bolene) (Proc.), 465*

HOUSE, R. K. Diffuse interstitial myocarditis in children, 797*
HUGULEY, C. H. (*See* Massie, Huguley, and Stillerman), 799*
HULBERT, BERNARD, AND MEYER, HERMAN M. Primary amyloidosis of the heart, 604
HULL, EDGAR. The cause and effects of flow through defects of the atrial septum, 350
HULTGREN, H. N. Calcific disease of the aortic valve, 631*
HULTQUIST, GÖSTA T. (*See* Lind and Hultquist), 123
HURWITT, E. S. An experimental approach to the problem of increasing the blood supply to the lungs, 446*
HYEMAN, A. (*See* Bennett and Hyeman), 797*

I

IGLAUER, A. (*See* Green, Iglauer, and McGuire), 144*
IRWIN, H. R., AND WINSOR, T. Venous pressures in children in health and disease, 931*
IVY, A. C. (*See* Nelson and Ivy) (Proc.), 459*

J

JAMES, FREDERICK. (*See* Wolffe, Digilio, Dale, McGinnis, Donnelly, Plungian, Sprowls, James, Einhorn, and Werkheiser) (Proc.), 467*
JAQUES, L. B., AND RICKER, A. G. The relationship between heparin and clotting time, 625*
JARISCH, A., AND ZOTTERMAN, Y. Depressor reflexes from the heart, 447*
JASPER, W. H. (*See* Burns, Jr., Jasper, and Wakerlin) (Proc.), 478*
JOHNSON, A. D. (*See* Green, Johnson, Lobb, and Cusick), 136*
JONES, H. E., AND MARSHALL, A. G. Isolated (Fiedler's) myocarditis, 153*
JONES, S. H., YOUNGHUSBAND, O. Z., AND EVANS, J. A. Human parabiotic pygopagus twins with hypertension: report of a case with clinical, psychological, and endocrinological observations, 792*
JULIAN, O. C. (*See* De Takats, Julian, and Fowler), 638*

K

KALLNER, S. Thrombosis as a complication of internal diseases, 311*
KATZ, L. N., HORLICK, L., RODBARD, S., STAMLER, J., AND BOLENE, C. Development and metamorphosis of cholesterol-induced atherosclerosis in the chick. Effects of a restricted dietary intake and of cessation of cholesterol feeding (Proc.), 465*
——. (*See* Dauber, Horlick, and Katz), 25
——. (*See* Horlick and Katz), 336
——. (*See* Rodbard, Brown, and Katz), 863
——. (*See* Stamler, Bolene, Katz, Harris, Silber, Miller, and Akman) (Proc.), 466*
KAY, H. B. Ventricular complexes in heart block, 317*
KAYLOR, C. T. (*See* Robb, Kaylor, and Turman), 148*
KEATING, JOHN H., JR. (*See* Griswold and Keating, Jr.), 813
KEATING, RICHARD P. (*See* Wégria, Segers, Keating, and Ward), 90
KEELEY, J. L. Saddle embolus of the aorta: report of successful embolectomy, 139*
KEITH, NORMAN M. (*See* Hines, Jr., Farber, and Keith) (Proc.), 468*
KELLNER, AARON, CORRELL, JAMES W., AND LADD, ANTHONY T. Modification of experimental atherosclerosis by means of an intravenous detergents (Proc.), 460*
KENDALL, FORREST E., MEYER, WALTER, AND DAVIDSON, JACK D. A method for the estimation of 7-ketocholesterol in in serum (Proc.), 474*
——. (*See* Bevans, Davidson, and Kendall) (Proc.), 462*
——. (*See* Davidson, Abell, and Kendall) (Proc.), 462*
——. (*See* Steiner, Kendall, and Bevans), 34
KENNEY, D. (*See* McGee, Priest, and Kenney), 140*
KENT, SIDNEY P. (*See* Baker and Kent) (Proc.), 470*
KEPLER, E. J. (*See* Cluxton, Jr., Bennett, and Kepler), 452*
KERGIN, F. G., BEAN, D. M., AND PAUL, W. Anoxia during intrathoracic operations, 628*
KERR, W. J. Pathogenesis of rheumatic fever, 450*
KERT, MORLEY J., AND HOOBLER, SIBLEY W. Observations on the potential variations of the cavities of the right side of the human heart, 97
KESSLER, D. L., AND HINES, L. E. Hazards of thiocyanate therapy in hypertension, 627*
KETY, SEYMOUR S. Measurement of regional circulation by the local clearance of radioactive sodium, 321
KETY, S. S. (*See* Bing, Hammond, Handelsman, Powers, Spencer, Eckenhoff, Goodale, Hafkenschiel, and Kety), 1
KEYS, A. (*See* Brozek, Chapman, and Keys), 140*
KEYS, ANCEL. (*See* Simonson, Brozek, and Keys), 407
KINMONTH, J. B. Thromboangiitis obliterans. Results of sympathectomy and prognosis, 932*
KINNEY, T. D. (*See* Hellems, Haynes, Dexter, and Kinney), 449*
KIRK, E., AND KVORNING, S. A. The silica content of the aortic wall in arteriosclerosis (Proc.), 476*
KISSANE, R. W. (*See* Mahanna, Clark, and Kissane), 301
KISTIN, A. D. (*See* Thompson and Kistin), 137*
KLEIN, HOWARD A. (*See* Myers, Klein, and Hiratzka), 547, 837

KOERPERICH, G. (*See* Welti and Koerperich), 636*
KRAMER, M. L. (*See* Gold, Modell, Kwit, Shane, Dayrit, Kramer, Zahm, and Otto), 307*
KROH, ILEEN. (*See* Scott, Young, Zimmerman, and Kroh), 881
KRUSEN, F. H. (*See* Wakim, Gersten, Herrick, Elkins, and Krusen), 153*
KULKA, WILLIAM. Delayed death following contusion of the heart, 438
KVORNING, S. A. (*See* Kirk and Kvorning) (Proc.), 476*
KWIT, N. J. (*See* Gold, Modell, Kwit, Shane, Dayrit, Kramer, Zahm, and Otto), 307*

L

LACK, ARTHUR, ADOLPH, WILLIAM, RALSTON, WALTER, LEIBY, GEORGE, WINSOR, TRAVIS, AND GRIFFITH, GEORGE. Biomicroscopy of conjunctival vessels in hypertension, 654
LADD, ANTHONY T. (*See* Kellner, Correll, and Ladd) (Proc.), 460*
LADUE, J. S., MURISON, P. J., AND PACK, G. T. The use of tetraethylammonium bromide as a diagnostic test for pheochromocytoma, 924*
LAGERLOF, S. (*See* Frisk, Hammarström, Lagerlof, Werkö, Björkenheim, Holmgren, and Larsson), 934*
LAMPSON, R. S., SCHAEFFER, W. C., AND LINCOLN, J. R. Acute circulatory arrest from ventricular fibrillation for twenty-seven minutes with complete recovery, 142*
LARSSON, Y. (*See* Frisk, Hammarström, Lagerlof, Werkö, Björkenheim, Holmgren, and Larsson), 934*
LATONA, SALVATORE R., AND LEFEVRE, FAY. Relationship of Dicumarol absorption to gastric free hydrochloric acid, 743
LAUFMAN, H., MARTIN, W. B., AND TANTURI, C. Effect of heparin and Dicumarol on sludge formation, 445*
LAWSON, H. C. (*See* Moore, Schadle, and Lawson), 314*
LAZARUS, S., MUNRO, H. N., AND BELL, G. H. Capillary strength tests in scurvy and their reactions to vitamin C and vitamin P therapy, 309*
LAZZARI, G. Acute malignant endocarditis from pneumococcus, 635*
LEEDS, F. H. (*See* Freeman, Leeds, and Gardner), 329
LEFEVRE, FAY. (*See* LaTona and LeFevre), 743
LEIBY, GEORGE. (*See* Lack, Adolph, Ralston, Leiby, Winsor, and Griffith), 654
LEINWAND, IRVING, AND MOORE, DAN H. Simultaneous studies on the serum lipids and the electrophoretic pattern of the serum protein in man: (1) action of inositol and other substances (Proc.), 467*
LENOX, B. (*See* Harrison and Lenox), 316*
LEONARDS, J. R. (*See* Williams and Leonards), 146*
LEROY, G. V., AND NALEFSI, L. A. Dicumarol in experimental myocardial infarction, 145*
LEVINE, H. D. Abnormal rapid rhythms associated with digitoxin therapy, 799*
LIAN, C., AND GERBAUX, A. Electric shock and auricular fibrillation, 636*
LILIENTHAL, J. L., JR. (*See* Folk, Zierler, and Lilienthal, Jr.), 315*
LINCOLN, J. R. (*See* Lampson, Schaeffer, and Lincoln), 142*
LIND, JOHN, AND HULTQUIST, GÖSTA T. Isolated myocarditis in newborn and young infants, 123
LITTMANN, D. Abnormal electrocardiograms in the absence of demonstrable heart disease, 149*
LOBB, A. (*See* Green, Johnson, Lobb, and Cusick), 136*
LOEWE, L. (*See* Morrison, Richter, and Loewe), 794*
LOHMAN, A. J. M. Mediastinitis anterior chronica, 629*
LONG, JOAN. (*See* Durant, Oppenheimer, Webster, and Long), 481
LONG, R. U. (*See* Meads, Long, Pace, and Harrell), 926*
LONG, W. K. (*See* Bloomfield, Rapoport, Milnor, Long, Mebane, and Ellis), 155*
LOUTIT, J. F. (*See* Barnes, Loutit, and Reeve), 630*, 631*
LUBSCHEZ, R. Immunologic and biochemical studies in infants and children with special reference to rheumatic fever. V. Electrophoretic patterns in blood plasma and serum in normal children, 931*
——. (*See* Wilson and Lubschez), 926*, 931*
——. (*See* Wilson, Payson, and Lubschez), 135*
LUISADA, A., AND FLEISCHNER, F. G. Studies of fluorocardiography: tracings of the left ventricle in myocardial infarction, 308*
LYON, THOMAS P. (*See* Sokolow and Lyon), 273
LYONS, C. (*See* Mayerson, Lyons, Parson, Nieset, and Trautman, Jr.), 798*
——. (*See* Parson, Mayerson, Lyons, Porter, and Trautman, Jr.), 798*

M

MCALLISTER, W. B., AND WATERS, L. L. Vascular lesions in the dog following thyroidectomy and viosterol feeding (Proc.), 463*
MACCARTY, C. S. (*See* Morgan, Allen, and MacCarty), 444*
MCCLURE, R. D., BEHRMANN, V. G., AND HARTMAN, F. W. The control of anoxemia during surgical anesthesia with the aid of the oxyhemograph, 623*
MCDONALD, J. R. (*See* Edwards, Christensen, Clagett, and McDonald), 633*

McDONALD, ROGER K., SOLOMON, DAVID H., AND SHOCK, NATHAN W. Ageing as a factor in the renal hemodynamic response to a standardized pyrogen test (Proc.), 476*

McEACHERN, D. (*See* Rabinovitch, Elliott, and McEachern), 135*

McGEE, C. J., PRIEST, W. S., AND KENNEY, D. Subacute bacterial endocarditis due to *Hemophilus parainfluenzae*, 140*

McGINNIS, GEORGE E. (*See* Wolffe, Digilio, Dale, McGinnis, Donnelly, Plungian, Sprowls, James, Einhorn, and Werkheiser) (Proc.), 467*

McGUIRE, J. (*See* Courter, Felson, and McGuire), 795*

——. (*See* Green, Iglauer, and McGuire), 144*

MACHT, D. I. Penicillin, streptomycin, Dicumarol and blood coagulation: thromboplastic properties of penicillin antibiotics, 148*

McKEOWN, C. E. (*See* Scotti and McKeown), 638*

McMANUS, J. F. A. Glomerular obsolescence in arteriosclerosis; identity and significance (Proc.), 475*

McMILLAN, G. C., AND DUFF, G. L. Mitotic activity in the aortic lesions of experimental cholesterol atherosclerosis of rabbits, 635*

MAHANNA, DONALD L., CLARK, THOMAS E., AND KISSANE, R. W. Auricular flutter during the administration of cyclopropane and curare, 301

MALINOW, M. R., MOIA, B., OTERO, E., AND ROSENBAUM, M. The occurrence of paroxysmal hypertension in patients with intermittent claudication, 702

MARCUS, H. R. (*See* Friedfeld, Marcus, and Vorzimer), 443*

MARCUS, LOUIS J. (*See* Goodman, Wasserman, Marcus, and Frankel) (Proc.), 475*

MARSHALL, A. G. (*See* Jones and Marshall), 153*

MARTIN, W. B. (*See* Laufman, Martin, and Tanturi), 445*

MARX, L. (*See* Deuel, Jr., Marx, Alfin-Slater, and Marx) (Proc.), 463*

MARX, LORE. (*See* Marx and Marx) (Proc.), 473*

MARX, W. (*See* Deuel, Jr., Marx, Alfin-Slater, and Marx) (Proc.), 463*

MARX, WALTER, AND MARX, LORE. Thyroid activity and tissue cholesterol distribution (Proc.), 473*

MASINI, V. (*See* Mussafia and Masini), 635*

MASSEY, F. C., AND DRAKE, W. L., JR. Spontaneous rupture of the heart due to myocardial infarction, 797*

MASSIE, E., HUGULEY, C. H., AND STILLERMAN, H. S. The heart in the terminal state: effect of intracardiac epinephrine, 799*

MASSON, G., GLASSER, O., SAVARD, K., CORCORAN, A. C., AND PAGE, IRVINE H. Fat tolerance curves in rat and rabbit using I^{131} (Proc.), 479*

MASSON, GEORGES. (*See* Corcoran, Masson, Hazard, and Page) (Proc.), 464*

MATHEWS, F. P. Enterococcal endocarditis, 147*

MAYERSON, H. S., LYONS, C., PARSON, WM., NIESET, R. T., AND TRAUTMAN, W. V., JR. Comparison of results of measurements of red blood cell volume by direct and indirect techniques, 798*

——. (*See* Parson, Mayerson, Lyons, Porter, and Trautman, Jr.), 798*

MEADS, M., LONG, R. U., PACE, S. H., AND HARRELL, G. T. Caronamide and penicillin: serum levels in human beings, following multiple doses of the drugs, 926*

MEBANE, J. G. (*See* Bloomfield, Rapoport, Milnor, Long, Mebane, and Ellis), 155*

MEGIBOW, R. S., POLLACK, H., MEGIBOW, S. J., BOOKMAN, J. J., AND OSSERMAN, K. The vascular problem in diabetes mellitus (Proc.), 468*

MEGIBOW, S. J. (*See* Megibow, Pollack, Megibow, Bookman, and Osserman) (Proc.), 468*

MELVILLE, K. I. Further studies on the antifibrillatory action of coronary dilator drugs, 627*

MENDLOWITZ, M. The effect of anemia and polycythemia on digital intravascular blood viscosity, 155*

MENEELY, JOHN K., JR. (*See* Beebe and Meneely, Jr.), 788

MENTEN, M. L., AND FETTERMAN, G. H. Coronary sclerosis in infancy, 448*

MESSER, ADDISON L., DONEGAN, CHARLES K., AND ORGAIN, EDWARD S. The influence of vagal activity on heart block, 732

MEYER, HERMAN M. (*See* Hulbert and Meyer), 604

MEYER, JACOB. (*See* Necheles, Meyer, and Becker) (Proc.), 472*

MEYER, P., AND HERR, R. Clinical and experimental observations on precordial leads and on the changing electrical field and the spontaneous electrical axes. Remarks on the doublet theory and the nature of the extrinsic and intrinsic deflection, 636*

——, AND ——. The electrical axis of standard and thoracic leads obtained by means of an artificial dipole, 632*

MEYER, WALTER. (*See* Kendall, Meyer, and Davidson) (Proc.), 474*

MICHEL, J. (*See* Soulie, Michel, and Baygin), 632*

MILLER, A. J. (*See* Stamler, Bolene, Katz, Harris, Silber, Miller, and Akman) (Proc.), 466*

MILLER, GEORGE V. (*See* Hejtmancik, Bradfield, Jr., and Miller), 757

MILNOR, J. P. (*See* Bloomfield, Rapoport, Milnor, Long, Mebane, and Ellis), 155*

MODELL, W. (*See* Gold, Modell, Kwit, Shane, Davrit, Kramer, Zahm, and Otto), 307*

MOE, T. (*See* Rasmussen and Moe), 315*

MOIA, B. (*See* Malinow, Moia, Otero, and Rosenbaum), 702

MOORE, DAN H. (*See* Leinwand and Moore) (Proc.), 467*

MOORE, J. C., SCHADLE, O. W., AND LAWSON, H. C. Measurement of the circulating red cell volume with methemoglobin-tagged cells, 314*

MOORE, R. L. Treatment of an infant with paroxysmal auricular tachycardia, 444*

MORGAN, E. H., ALLEN, E. V., AND MACCARTY, C. S. Acute peripheral circulatory failure caused by acute venous thrombosis, 444*

MORIYAMA, I. M. (*See* Woolsey and Moriyama), 445*

MORRISON, LESTER M., AND GONZALEZ, WILLIAM F. Results of treatment of coronary arteriosclerosis with choline (Proc.), 471*

——, BERLIN, PERLA, AND GONZALEZ, WILLIAM F. Fat tolerance tests in coronary thrombosis (Proc.), 477*

——, CHANEY, ALBERT L., GONZALEZ, WILLIAM, AND BERLIN, PERLA. Metabolic studies in coronary thrombosis (Proc.), 477*

——, HALL, LILLIAN, AND GONZALEZ, WILLIAM F. The significance of blood serum cholesterol instability in coronary arteriosclerosis (Proc.), 478*

MORRISON, M., RICHTER, I. H., AND LOEWE, L. Increased platelet clumping in thromboembolic disease, 794*

MORTENSEN, V., AND WARBURG, E. Chronic constrictive pericarditis, 630*

MOWBRAY, R., AND BOWLEY, C. C. Congenital complete heart block complicating pregnancy, 146*

MOYER, J. H., AND ACKERMAN, A. J. Hereditary hemorrhagic telangiectases associated with pulmonary arteriovenous fistula in two members of a family, 799*

MUFSON, I. A new treatment for the relief of obliterative disease of peripheral arteries, 924*

MUNRO, H. N. (*See* Lazarus, Munro, and Bell), 309*

MURISON, P. J. (*See* LaDue, Murison, and Pack), 924*

MURRAY, G. Closure of defects in cardiac septa, 624*

MUSSAFIA, A., AND MASINI, V. Prognosis in myocardial infarction. I. Prognosis after the acute stage, 635*

MYERS, GORDON B., KLEIN, HOWARD A., AND HIRATZKA, TOMIHARU. V. Correlation of electrocardiographic and pathologic findings in posterior infarction, 547

——, ——, AND ——. VI. Correlation of electrocardiographic and pathologic findings in posterolateral infarction, 837

MYERS, J. D., AND HICKAM, J. B. An estimation of the hepatic blood flow and splanchnic oxygen consumption in heart failure, 306*

MYERSON, A. (*See* Hauptmann and Myerson), 145*

MYLON, E., AND FREEDMAN, L. R. On the occurrence of renin in the blood of hypertensive patients, 509

N

NAHUM, L. H., AND HOFF, H. E. Nature of the precordial electrocardiogram, 798*

NALEFSI, L. A. (*See* LeRoy and Nalefsi), 145*

NECHELES, H., MEYER, JACOB, AND BECKER, G. H. Fat absorption and atherosclerosis. A theory on the development of atherosclerosis with ageing (Proc.), 472*

NELSON, DOROTHY, AND IVY, A. C. Observations on the experimental production of arteriosclerosis in the guinea pig (Proc.), 459*

NELSON, H. G., AND THE PERSONNEL OF UNITED STATES NAVAL MEDICAL RESEARCH UNIT. 4. Studies on rheumatic fever: observations on tonsillar carriers of hemolytic streptococci; the effect of tonsillectomy and the administration of penicillin on rheumatic and nonrheumatic fever patients, 306*

NEWMAN, M. Coarction of the aorta, 316*

NIESET, R. T. (*See* Mayerson, Lyons, Parson, Nieset, and Trautman, Jr.), 798*

NITSCH, EMILIA. (*See* Sinclair, Jr., and Nitsch), 898

NOBLE, R. P. (*See* Hamilton, Riley, Attyah, Cournand, Fowell, Himmelstein, Noble, Remington, Richards, Jr., Wheeler, and Witham), 314*

NORMAN, L. R. (*See* Harken, Ellis, Ware, and Norman), 932*

O

OCHSNER, A. Venous thrombosis, 638*

OPPENHEIMER, M. J. (*See* Durant, Oppenheimer, Webster, and Long), 481

ORGAIN, EDWARD S. (*See* Messer, Donegan, and Orgain), 732

OSBORN, S. B. (*See* Wright, Osborn, and Edmonds), 932*

OSSERMAN, K. (*See* Megibow, Pollack, Megibow, Bookman, and Osserman) (Proc.), 468*

OTERO, E. (*See* Malinow, Moia, Otero, and Rosenbaum), 702

OTTO, H. L. (*See* Gold, Modell, Kwit, Shane, Davrit, Kramer, Zahm, and Otto), 307*

P

PACE, J. M. (*See* Sweeney and Pace), 138*

PACE, S. H. (*See* Meads, Long, Pace, and Harrell), 926*

PACK, G. T. (*See* LaDue, Murison, and Pack), 924*
PACKARD, G. B., AND WARING, J. J. Arteriovenous fistula of the lung, 315*
PAGE, I. H. (*See* Rapport, Green, and Page), 445*
PAGE, IRVINE H. On certain aspects of the nature and treatment of oligemic shock, 161
——. (*See* Brown and Page) (Proc.), 479*
——. (*See* Corcoran, Masson, Hazard, and Page) (Proc.), 464*
——. (*See* Masson, Glasser, Savard, Corcoran, and Page) (Proc.), 479*
PALMER, J. L., AND GUNDERSON, S. M. The effect of Dicumarol on the erythrocyte sedimentation rate in normal men, 933*
PANTRIDGE, J. FRANK. Cardiac lesions in thiamine deficiency, 639*
PARKER, R. L., AND BARKER, N. W. The effect of anticoagulants on the incidence of thromboembolic complications in acute myocardial infarction, 636*
PARSON, WM., MAYERSON, H. S., LYONS, C., PORTER, B., AND TRAUTMAN, W. V., JR. Effect of the administration of adrenalin on the circulating red cell volume, 798*
——. (*See* Mayerson, Lyons, Parson, Nieset, and Trautman, Jr.), 798*
PATERSON, J. C., AND COTTRALL, G. E. The etiology of coronary sclerosis in chickens (Proc.), 466*
PATTERSON, M. C. (*See* Blood and Patterson), 628*
PAUL, W. (*See* Kergin, Bean, and Paul), 628*
PAYNE, TORRENCE P. B. (*See* Duff and Payne) (Proc.), 460*
PAYSON, J. W. (*See* Wilson, Payson, and Lubschez), 135*
PEEL, F. A. A. Tuberculous pericarditis, 317*
PETERS, J. P. The role of sodium in the production of edema, 318*
PICCIONE, F. V. (*See* Erf, Foldes, Piccione, and Wagner, Jr.), 766
PLUNGIAN, MIKHAIL B. (*See* Wolffe, Digilio, Dale, McGinnis, Donnelly, Plungian, Sprowls, James, Einhorn, and Werkheiser) (Proc.), 467*
POKRESS, MURRAY J., AND GOLDBERGER, EMANUEL. A study of the Q-T interval in rheumatic fever, 423
POLLACK, H. (*See* Megibow, Pollack, Megibow, Bookman, and Osserman) (Proc.), 468*
POLLAK, O. J. Rapid production of atheromatosis in rabbits (Proc.), 459*
——. (*See* Goldman and Pollak) (Proc.), 474*
POLLEY, J. R. (*See* Friedman, Friedman, and Polley), 313*
PORTER, B. (*See* Parson, Mayerson, Lyons, Porter, and Trautman, Jr.), 798*
PORTER, W. B. The probably grave significance of premature beats occurring in angina pectoris induced by effort, 795*
POTTS, W. J., GIBSON, S., AND ROTHWELL, R. Double aortic arch, 635*
POWERS, S. R. (*See* Bing, Hammond, Handelsman, Powers, Spencer, Eckenhoff, Goodale, Hafkenschiel, and Kety), 1
PRATT, GERALD H. Surgical treatment of aneurysms, 43
PRIEST, W. S. (*See* McGee, Priest, and Kenney), 140*
PRINZMETAL, M., CORDAY, E., BERGMAN, H. C., SCHWARTZ, L., AND SPRITZLER, R. J. Radiocardiography: a new method for studying the blood flow through the chambers of the heart in human beings, 445*
——. (*See* Simkin, Bergman, Silver, and Prinzmetal), 310
PROUDFIT, WILLIAM L. (*See* Ernstene and Proudfit), 260
PRYCE, D. M. (*See* Barnes, Fatti, and Pryce), 446*
PUGH, D. H. The value of roentgen diagnosis in coarctation of the aorta, 663*

R

RABINOVITCH, R., ELLIOTT, K. A. C., AND MCEACHERN, D. Cytochrome C: intravenous administration in man, 135*
RACE, GEORGE G., AND BLACK-SCHAFFER, BERNARD. Idiopathic infantile hyperplastic and hypertrophic cardiomegaly (congenital cardiac hypertrophy), 501
RALSTON, WALTER. (*See* Lack, Adolph, Ralston, Leiby, Winsor, and Griffith), 654
RAPEE, L. A. (*See* Bageant and Rapee), 151*
RAPOPORT, B. (*See* Bloomfield, Rapoport, Milnor, Long, Mebane, and Ellis), 155*
RAPOPORT, S. (*See* Stead, Reiser, Rapoport, and Ferris), 928*
RAPPAPORT, MAURICE B. (*See* Wells, Rappaport, and Sprague), 69
RAPPORT, M. M., GREEN, A. A., AND PAGE, I. H. Crystalline serotonin, 445*
RASMUSSEN, H., AND MOE, T. Pathogenesis of left bundle branch block, 315*
RAWSON, A. J. (*See* DeMuth and Rawson), 137*
REEVE, E. B. (*See* Barnes, Loutit, and Reeve), 630*, 631*
REISER, M. F. (*See* Stead, Reiser, Rapoport, and Ferris), 928*
REMINGTON, J. W. (*See* Briggs, Fowell, Hamilton, Remington, Wheeler, and Winslow), 928*
——. (*See* Hamilton and Remington), 313*
——. (*See* Hamilton, Riley, Attyah, Cournand, Fowell, Himmelstein, Noble, Remington, Richards, Jr., Wheeler, and Witham), 314*
RENARD, C. H. (*See* Roskam, Renard, and Swalue), 624*
RICHARDS, D. W., JR. (*See* Hamilton, Riley, Attyah, Cournand, Fowell, Himmelstein, Noble, Remington, Richards, Jr., Wheeler, and Witham), 314*
RICHTER, I. H. (*See* Morrison, Richter, and Loewe), 794*
RICKER, A. G. (*See* Jaques and Ricker), 625*

RIGLER, L. (*See* Shapiro and Rigler), 450*
RILEY, R. L. (*See* Hamilton, Riley, Attyah, Cournand, Fowell, Himmelstein, Noble, Remington, Richards, Jr., Wheeler, and Witham), 314*
ROBB, J. S., KAYLOR, C. T., AND TURMAN, W. G. A study of specialized heart tissue at various stages of development of the human fetal heart, 148*
RODBARD, S., BROWN, F., AND KATZ, L. N. The pulmonary arterial pressure, 863
——. (*See* Katz, Horlick, Rodbard, Stamler, and Bolene) (Proc.), 465*
RODRIGUEZ, R., AND ROOT, H. F. Capillary fragility and diabetic retinitis, 312*
ROOT, H. F. (*See* Rodriguez and Root), 312*
ROSE, O. A. (*See* DeGraff, Batterman, and Rose), 626*
ROSENBAUM, FRANCIS F. (*See* Topp and Rosenbaum), 130
ROSENBAUM, M. (*See* Malinow, Moia, Otero, and Rosenbaum), 702
ROSENBERG, B., ROSENTHAL, A. E., AND ROSENBLUTH, M. B. Effect of the low sodium diet and the rice diet on arterial blood pressure, 934*
ROSENBERG, CONRAD, AND SCHLOSS, BENJAMIN. Plasma hexosamine levels in acute rheumatic fever, 872
ROSENBLUTH, M. B. (*See* Rosenberg, Rosenthal, and Rosenbluth), 934*
ROSENBURG, MARVIN J., AND AGRESS, CLARENCE M. Position of precordial leads, 593
ROSENBURG, M. J. Subacute bacterial endocarditis: report of a case of reinfection, 927*
ROSENTHAL, A. E. (*See* Rosenberg, Rosenthal, and Rosenbluth), 934*
ROSKAM, J., RENARD, C. H., AND SWALUE, L. Inconstancy and variability of the vascular fragility test even in purpuric conditions, 624*
ROTH, OSCAR, AND DOFF, SIMON D. Electrocardiograms of an unusual pattern in a patient with anomalous auriculoventricular excitation, 614
ROTHWELL, R. (*See* Potts, Gibson, and Rothwell), 635*

S

SALASSA, R. M., BOLLMAN, J. L., AND DRY, T. J. The effect of para-aminobenzoic acid on the metabolism and excretion of salicylate, 929*
SAMPSON, JOHN J., AND SINGER, ISADORE M. Plasma and blood infusion following myocardial infarction, 54
SANCETTA, SALVATORE M. (*See* Scott and Sancetta), 747
SAVARD, K. (*See* Masson, Glasser, Savard, Corcoran, and Page) (Proc.), 479*
SAŸEN, JOHN J., AND SHELDON, WARNER F. The heart muscle and the electrocardiogram in coronary disease. II. Difficulties of description and illustration of ventricular muscle lesions, with a method for their graphic representation in a myocardial map, 688
——. (*See* Sheldon and Saÿen), 517
SCHADLE, O. W. (*See* Moore, Schadle, and Lawson), 314*
SCHAEFFER, W. C. (*See* Lampson, Schaeffer, and Lincoln), 142*
SCHILDGE, E. (*See* Berg, Delius, and Schildge), 309*
SCHLESINGER, MONROE J., ZOLL, PAUL M., AND WESSLER, STANFORD. The conus artery: a third coronary artery, 823
SCHLICHTER, J. G. (*See* Amromin, Schlichter, and Solway), 639*
——, WILBURNE, M., AND GROSSMAN, M. The use of acetylcholine in the objective determination of circulation time in man, 796*
SCHLOSS, BENJAMIN. (*See* Rosenburg and Schloss), 872
SCHROEDER, H. A. (*See* Williams and Schroeder), 449*
SCHWARTZ, L. (*See* Prinzmetal, Corday, Bergman, Schwartz, and Spritzler), 445*
SCOTT, ROY W., AND SANCETTA, SALVATORE M. Dissecting aneurysm of aorta with hemorrhagic infarction of the spinal cord and complete paraplegia, 747
SCOTT, R W., YOUNG, A. F., ZIMMERMAN, H. A., AND KROH, ILEEN. An improved method for visualizing the coronary arteries at post mortem, 881
SCOTT, W. G. (*See* Carson, Burford, Scott, and Goodfriend), 930*
SCOTTI, T. M., AND MCKEOWN, C. E. Sarcoidosis involving the heart in a case of sudden death, 638*
SEGERS, MARCEL. (*See* Wégria, Segers, Keating, and Ward), 90
SEITUN, F. (*See* Grossi and Seitun), 792*
SELZER, A. The immediate sequelae of myocardial infarction, 136*
SHANE, S. J. (*See* Gold, Modell, Kwit, Shane, Davrit, Kramer, Zahm, and Otto), 307*
SHAPIRO, R., AND RIGLER, L. Pulmonary embolism without infarction, 450*
SHEA, E. (*See* D'Alton, Darling, and Shea), 795*
SHELDON, WARNER F., AND SAŸEN, JOHN J. The heart muscle and the electrocardiogram in coronary disease. I. Survey of standards and methods for obtaining the anatomic data requisite for clinicopathologic correlation, 517
——. (*See* Saÿen and Sheldon), 688
SHEPHARD, E. M. (*See* Steward, Shephard, and Horger), 934*
SHIPLEY, R. E., AND HELMER, O. M. Observa tions on the "sustained pressor prin ciple" in different animal species, 314*
SHOCK, NATHAN W. (*See* McDonald, Solomon, and Shock) (Proc.), 476*
SHORT, D. W. Occupational aneurysm of the palmer arch, 147*
SHUMACKER, H. B. Causalgia. III. A general discussion, 638*
SIGLER, L. H. Subjective manifestations of the hyperactive carotid sinus reflex, 452*

SILBER, E. N. (*See* Stamler, Bolene, Katz, Harris, Silber, Miller, and Akman) (Proc.), 466*
SILVER, H. (*See* Simkin, Bergman, Silver, and Prinzmetal), 310*
SIMKIN, B., BERGMAN, H. C., SILVER, H., AND PRINZMETAL, M. Renal arteriovenous anastomoses in rabbits, dogs, and human subjects, 310*
SIMMS, HENRY S. Further studies on the action of antilipfanogen in preventing fat deposition (Proc.), 465*
SIMONSON, ERNST, BROZEK, JOSEF, AND KEYS, ANCEL. Variability of the electrocardiogram in normal young men, 407
SINCLAIR, WILLIAM, JR., AND NITSCH, EMILIA. Polyarteritis nodosa of the coronary arteries, 898
SINGER, ISADORE M. (*See* Sampson and Singer), 54
SLAUGHTER, O. (*See* Wakim, Slaughter, and Clagett), 634*
SLOAN, ROBERT D. (*See* Bahnson, Cooley, and Sloan), 905
SMITH, BEVERLY C. The use of radioactive sodium in the diagnosis of peripheral circulation in peripheral arteriosclerosis (Proc.), 469*
SMITH, R. G., AND CAMPBELL, D. A. Some technical considerations in the arteriographic examination of the lower extremity, 793*
SMULL, K., WISSLER, R. W., AND WATSON, J. M. The effect of sodium salicylate upon serum disease in rabbits, 143*
SOKOLOW, MAURICE, AND FRIEDLANDER, RICHARD D. The normal unipolar precordial and limb lead electrocardiogram, 665
——, AND LYON, THOMAS P. The ventricular complex in right ventricular hypertrophy as obtained by unipolar precordial and limb leads, 273
SOLOMON, DAVID H. (*See* McDonald, Solomon, and Shock) (Proc.), 476*
SOLWAY, A. J. L. (*See* Amromin, Schlichter, and Solway), 639*
SORGO, W. The intramedullary section of vasomotor pathways as treatment of arterial hypertension, 447*
SOULIE, P., MICHEL, J., AND BAYGIN, R. High precordial leads in normal subjects and in patients with coronary artery disease, 632*
SPENCER, F. C. (*See* Bing, Hammond, Handelsman, Powers, Spencer, Eckenhoff, Goodale, Hafkenschiel, and Kety), 1
SPICKNALL, CHARLES G. (*See* Dorset, Spicknall, and Terry), 610
SPRAGUE, HOWARD B. (*See* Wells, Rappaport, and Sprague), 69
SPRITZLER, R. J. (*See* Prinzmetal, Corday, Bergman, Schwartz, and Spritzler), 445*
SPROWLS, JOSEPH. (*See* Wolffe, Digilio, Dale, McGinnis, Donnelly, Plungian, Sprowls, James, Einhorn, and Werkheiser) (Proc.), 467*
STAMLER, J., BOLENE, C., KATZ, L. N., HARRIS, R., SILBER, E. N., MILLER, A. J., AND AKMAN, L. Studies on spontaneous and cholesterol-induced atherosclerosis and lipid metabolism in the chick. The effects of some lipotropic and hormonal factors (Proc.), 466*
——. (*See* Katz, Horlick, Rodbard, Stamler, and Bolene) (Proc.), 465*
STANSFIELD, H. (*See* Hoff and Stansfield), 193
STEAD, W. W., REISER, M. F., RAPOPORT, S., AND FERRIS, E. B. The effect of sodium chloride depletion on blood pressure and tetraethylammonium chloride response in hypertension, 928*
STEINER, ALFRED, KENDALL, FORREST E., AND BEVANS, MARGARET. Production of arteriosclerosis in dogs by cholesterol and thiouracil feeding, 34
STEWARD, H. J., SHEPHARD, E. M., AND HORGER, E. L. Electrocardiographic manifestations of potassium intoxication, 934*
STILLERMAN, H. S. (*See* Massie, Huguley, and Stillerman), 799*
STONER, H. B. (*See* Wilson and Stoner), 629*
SURTSHIN, A. (*See* Horlick and Surtshin), 716
SWALUE, L. (*See* Roskam, Renard, and Swalue), 624*
SWAN, HENRY. Mitral stenosis: an experimental study of pulmonary-azygos venous anastomosis, 367
——, TRAPNELL, J. M., AND DENST, JOHN. Congenital mitral stenosis and systemic right ventricle with associated pulmonary vascular changes frustrating surgical repair of patent ductus arteriosus and coarctation of the aorta, 914
SWEENEY, J. S., AND PACE, J. M. Hypertension caused by unilateral kidney disease (a follow-up report), 138*
SZILAGYI, N. (*See* Taren and Szilagyi), 150*

T

DE TAKATS, GEZA, AND FOWLER, EDSON F. The water tolerance of the hypertensive patient; its relation to operability, 234
——. See also under D
TANNENBAUM, W. J. (*See* Bettman and Tannenbaum), 925*
TANTURI, C. (*See* Laufman, Martin, and Tanturi), 445*
TARAN, L. M., AND SZILAGYI, N. Effect of oxygen therapy on the electrical sequence of events in the cardiac cycle in children with acute rheumatic carditis, 150*
——, AND ——. Oxygen therapy in acute rheumatic carditis in children, 150*
TAYLOR, C. BRUCE, BALDWIN, DAVID, AND HAAS, GEORGE M. Histologic sequences of degeneration and repair of the rabbit aorta following hypothermal injury (Proc.), 464*
TERRY, LUTHER L. (*See* Dorset, Spicknall, and Terry), 610

THOMAS, EVAN W. (*See* Flaum and Thomas), 361
THOMAS, S. F., ALTO, P., AND GARLAND, L. H. Roentgen cardiac kymography; electrocardiographic correlation, 311*
THOMPSON, J. L., JR., AND KISTIN, A. D. Hoarseness in heart disease, 137*
THORNER, M. C., CARTER, R. A., AND GRIFFITH, GEORGE C. Calcification as a diagnostic sign of syphilitic aortitis, 641
TOPP, JAMES H., AND ROSENBAUM, FRANCIS F. A device for measuring the mean electrical axis of the heart, 130
TRAPNELL, J. M. (*See* Swan, Trapnell, and Denst), 914
TRAUTMAN, W. V., JR. (*See* Mayerson, Lyons, Parson, Nieset, and Trautman, Jr.), 798*
——. (*See* Parson, Mayerson, Lyons, Porter, and Trautman, Jr.), 798*
TRIMBLE, G. X. Ventricular irregularities induced by sympathoadrenal discharge and chloroform, 930*
TURMAN, W. G. (*See* Robb, Kaylor, and Turman), 148*

V

VALENCIA, FERNANDO. (*See* Barker and Valencia), 376
VAN WYK, J. J., AND HOFFMANN, C. R. Periarteritis nodosa, 631*
VORZIMER, J. J. (*See* Friedfeld, Marcus, and Vorzimer), 443*
DE VRIES, A., AND HALPERN, L. Unusual features in a case of carotid sinus syndrome, 295

W

WAGNER, F. B., JR. (*See* Erf, Foldes, Piccione, and Wagner, Jr.), 766
WAKERLIN, G. E. (*See* Burns, Jr., Jasper, and Wakerlin) (Proc.), 478*
WAKIM, K. G., GERSTEN, J. W., HERRICK, J. F., ELKINS, E. C., AND KRUSEN, F. H. The effects of diathermy on the flow of blood in the extremities, 153*
——, SLAUGHTER, O., AND CLAGETT, O. T. Studies on the blood flow in the extremities in cases of coarctation of the aorta: determinations before and after excision of the coarctate region, 634*
WALLS, E. W. The regenerative capacity of mammalian heart muscle, 317*
WANG, C. H., BLAND, E. F., AND WHITE, P. D. A note on coronary occlusion and myocardial infarction found post mortem at the Massachusetts General Hospital during the twenty year period from 1926 to 1945 inclusive, 451*
WARBURG, E. (*See* Mortensen and Warburg), 630*
WARD, HENRY P. (*See* Wégria, Segers, Keating, and Ward), 90
WARE, P. F. (*See* Harken, Ellis, Ware, and Norman), 932*
WARING, J. J. (*See* Packard and Waring), 315*
WARNER, E. D. (*See* Boyd and Warner), 930*
WASSERMAN, SIGMUND. (*See* Goodman, Wasserman, Marcus, and Frankel) (Proc.), 475*
WATERS, L. L. (*See* McAllister and Waters) (Proc.), 463*
WATSON, J. M. (*See* Smull, Wissler, and Watson), 143*
WEBSTER, M. R. (*See* Durant, Oppenheimer, Webster, and Long), 481
WÉGRIA, RENÉ, SEGERS, MARCEL, KEATING, RICHARD P., AND WARD, HENRY P. Relationship between the reduction in coronary flow and the appearance of electrocardiographic changes, 90
WEINSTEIN, MAY S., AND ARATA, JUSTIN E. Mitral stenosis and insufficiency produced by cardiac "myxoma," 781
WELLS, BERTRAND G., RAPPAPORT, MAURICE B., AND SPRAGUE, HOWARD B. The sounds and murmurs in coarctation of the aorta, 69
WELTI, J. J., AND KOERPERICH, G. The prognosis of patent ductus arteriosus in fifty-four nonoperated cases, 636*
WERKHEISER, GEORGE. (*See* Wolffe, Digilio, Dale, McGinnis, Donnelly, Plungian, Sprowls, James, Einhorn, and Werkheiser) (Proc.), 467*
WERKÖ, L. (*See* Frisk, Hammarström, Lagerlof, Werkö, Björkenheim, Holmgren, and Larsson), 934*
WESSLER, STANFORD. (*See* Schlesinger, Zoll, and Wessler), 823
WHEELER, N. C. (*See* Briggs, Fowell, Hamilton, Remington, Wheeler, and Winslow), 928*
——. (*See* Hamilton, Riley, Attyah, Cournand, Fowell, Himmelstein, Noble, Remington, Richards, Jr., Wheeler, and Witham), 314*
WHITE, J. C., HEROY, W. W., AND GOODMAN, E. N. Causalgia following gunshot injuries of nerves, 138*
WHITE, N. K., AND EDWARDS, J. E. Anomalies of the coronary arteries, 632*
WHITE, P. D. (*See* Evans and White), 794*
——. (*See* Wang, Bland, and White), 451*
WILBURNE, M. (*See* Schlichter, Wilburne, and Grossman), 796*
WILLIAMS, A. H., AND SCHROEDER, H. A. Asystolic arterial pressure gradient as a measure of local peripheral resistance, 449*
WILLIAMS, F., AND LEONARDS, J. R. The effect of sodium bicarbonate on the renal excretion of salicylate, 146*
WILSON, A., AND STONER, H. B. The effect of the injection of acetylcholine into the brachial artery of normal subjects and patients with myasthenia gravis, 629*
WILSON, M. G., AND LUBSCHEZ, R. Immunologic and biochemical studies in infants and children with special reference to rheumatic fever. VI. Electrophoretic patterns of blood plasma and serum in rheumatic children, 931*

——, AND ——. Longevity in rheumatic fever: based on experience of 1,042 children observed over a period of thirty years, 926*

——. Immunologic and biochemical studies in infants and children with special reference to rheumatic fever. I. The role of genetic susceptibility, 444*

——, PAYSON, J. W., AND LUBSCHEZ, R. Experience of rheumatic patients who served in the Armed Forces, 1942-46, 135*

WINSLOW, J. A. (*See* Briggs, Fowell, Hamilton, Remington, Wheeler, and Winslow), 928*

WINSOR, T. (*See* Irwin and Winsor), 931*

WINSOR, TRAVIS. (*See* Lack, Adolph, Ralston, Leiby, Winsor, and Griffith), 654

WISSLER, R. W. (*See* Smull, Wissler, and Watson), 143*

WITHAM, N. C. (*See* Hamilton, Riley, Attyah, Cournand, Fowell, Himmelstein, Noble, Remington, Richards, Jr., Wheeler, and Witham), 314*

WOLFF, G. Childhood mortality from rheumatic fever and heart diseases, 307*

WOLFFE, JOSEPH B., DIGILIO, VICTOR A., DALE, ANTHONY D., MCGINNIS, GEORGE E., DONNELLY, DANIEL J., PLUNGIAN, MIKHAIL B., SPROWLS, JOSEPH, JAMES, FREDERICK, EINHORN, CLAIRE, AND WERKHEISER, GEORGE. Experimental atheromatosis and atherohepatosis in ducks and geese; its reversibility and its clinical implications (Proc.), 467*

WOOD, E. H. (*See* Brown, Clagett, Burchell, and Wood), 634*

WOOLSEY, T. D., AND MORIYAMA, I. M. Statistical studies of heart disease. II. Important factors in heart disease mortality trends, 445*

WRIGHT, H. P., OSBORN, S. B., AND EDMONDS, D. G. Rate of flow of venous blood in the legs measured with radioactive sodium, 932*

Y

YOUNG, A. F. (*See* Scott, Young, Zimmerman, and Kroh), 881

YOUNGHUSBAND, O. Z. (*See* Jones, Younghusband, and Evans), 792*

Z

ZAHM, W. (*See* Gold, Modell, Kwit, Shane, Davrit, Kramer, Zahm, and Otto), 307*

ZEMAN, FREDERIC D. The principal syndromes associated with cerebralarteriosclerosis (Proc.), 471*

ZIEGLER, R. F. The cardiac mechanism during anesthesia and operation in patients with congenital heart disease and cyanosis, 153*

ZIERLER, K. L. (*See* Folk, Zierler, and Lilienthal, Jr.), 315*

ZIMMERMAN, H. A. (*See* Scott, Young, Zimmerman, and Kroh), 881

ZOLL, PAUL M. (*See* Schlesinger, Zoll, and Wessler), 823

ZOTTERMAN, Y. (*See* Jarisch and Zotterman), 447*

SUBJECT INDEX*

A

Abdominal aortic aneurysm, prognosis in, 470*

Acetylcholine, effect of injection of, into brachial artery of normal subjects and patients with myasthenia gravis, 629*

use of, in objective determination of circulation time in man, 796*

Adrenalin, effect of administration of, on circulating red cell volume, 798*

effects of, in normal and hypertensive patients in relation to mechanism of sustained pressure elevations, 136*

Air embolism, arterial (Durant et al.), 481

Alloxan diabetes in rabbit, studies on mechanism of inhibition of experimental cholesterol atherosclerosis in, 460*

American Heart Association, Inc., 158, 320, 453, 640, 800, 941

annual meeting, June 22-25, 1950, 640, 941

Arteriosclerosis, American Society for Study of, 453

electrocardiography, course in, 160

Executive Committee meeting, 800

Gerontological Society, annual meeting of, 453

Gold Award given at annual dinner, 159

grants for research in cardiovascular disease, 320

grants-in-aid, additional, 320

grants-in-aid for research, 800

Hawaii Heart Association admitted to AHA; Board approves $6,000,000 goal for 1950, 160

Heart Associations, new affiliated, 640

1950 Heart Campaign, A. W. Robertson chairman of, 800

High Blood Pressure, American Foundation for, becomes section on scientific control, 320

International Congress in 1950, 640

Life Insurance Medical Research Fund, 1950 research grants and fellowships of, 942

National conference on cardiovascular diseases to be held in Washington in January, 800

President, Dr. H. M. Marvin elected, at annual meeting in Atlantic City, 158

Program Committee, 941

Registry of Cardiovascular Pathology, cases solicited for, 942

Rheumatic Fever, American Council on, American Legion aid cited at meeting of, 160

Scientific Council elections, 453

University of Vermont, refresher course presented at, 454

American Heart Association, Inc.—Cont'd

Society for the Study of Arteriosclerosis, proceedings of, 459

program, 455

Aminophyllin determination of circulation time, 443*

effect of, on coagulation of human blood, 628*

Amyloidosis, primary, of heart (Hulbert and Meyer), 604

Anastomoses, renal arteriovenous, in rabbits, dogs, and human subjects, 310*

Anastomosis, venous, pulmonary-azygos, experimental stenosis (Swan), 367

Anemia and polycythemia, effect of, on digital intravascular blood viscosity, 155*

role of, in experimental production of heart block and auricular fibrillation in dog (Horlick and Surtshin), 716

Anesthesia and operation, cardiac mechanism during, in patients with congenital heart disease and cyanosis, 153*

surgical, control of anoxemia during, with aid of oxyhemograph, 623*

Aneurysm, aortic, abdominal, prognosis in, 470*

arteriovenous, of lung, 446*

dissecting, of aorta with hemorrhagic infarction of spinal cord and complete paraplegia (Scott and Sancetta), 747

occupational, of palmar arch, 147*

Aneurysms, surgical treatment of (Pratt), 43

Angina pectoris, case of, precipitated chiefly by tobacco smoking and meals (Ahn and Göhle), 775

induced by effort, probably grave significance of premature beats occurring in, 795*

Angiocardiography, diagnosis of pulmonary stenosis by, 930*

Announcement, 791, 822

Anoxemia during surgical anesthesia, control of, with aid of oxyhemograph, 623*

Anoxia during intrathoracic operations, 628*

Antifibrillatory action of coronary dilator drugs, further studies on, 627*

Antilipfanogen, further studies on action of, in preventing fat deposition, 465*

Aorta, changes in cutaneous arterioles in arm and leg in coarctation of, 468*

coarctation of, 316*

at unusual sites (Bahnson et al.), 905

congenital mitral stenosis and systemic right ventricle with associated pulmonary vascular changes frustrating surgical repair of patent ductus arteriosus and (Swan et al.), 914

dissecting aneurysm of, with hemorrhagic infarction of spinal cord and complete paraplegia (Scott and Sancetta), 747

*An asterisk (*) after a page number indicates the reference is an abstract and not an original article.

Aorta—Cont'd
medionecrosis of, 639*
near diaphragm, acquired coarctation of, 792*
pathologic considerations in coarctation of, 633*
pathology of intrapulmonary arteries and arterioles in coarctation of, associated with patent ductus arteriosus (Edwards et al.), 205
preoperative and postoperative studies of intraradial and intrafemoral pressures in patients with coarctation of, 634*
rabbit, histologic sequences of degeneration and repair of, following hypothermal injury, 464*
saddle embolus of; report of successful embolectomy, 139*
sounds and murmurs in coarctation of (Wells et al.), 69
studies on blood flow in extremities in cases of coarctation of: determinations before and after excision of coarctate region, 634*
surgical treatment and physiopathology of coarctation of, 623*
of coarctation of, 634*
value of roentgen diagnosis in coarctation of, 633*
Aortic aneurysm, abdominal, prognosis in, 470*
arch, double, 635*
embolism, 925*
valve, calcific disease of, 631*
wall, silica content of, in arteriosclerosis, 476*
Aortitis, syphilitic, calcification as diagnostic sign of (Thorner et al.), 641
Apoplexy, relation of cardiovascular disease to (Hicks and Black), 528
Arch, aortic, double, 635*
Arterectomy in treatment of intractable pain following recovery from acute arterial occlusion (Freeman et al.), 329
Arterial air embolism (Durant et al.), 481
disease, functional and organic, nail changes in, 443*
hypertension, effect of tetraethylammonium in, 934*
intramedullary section of vasomotor pathways as treatment of, 447*
occlusion, acute, arterectomy in treatment of intractable pain following recovery from (Freeman et al.), 329
pressure gradient, asystolic, as measure of local peripheral resistance, 449*
pulmonary (Rodbard et al.), 863
tissue, biology of, 461*
Arteries, coronary, improved method for visualizing, at post mortem (Scott et al.), 881
of newborn infants, necrosis in (Gruenwald), 889
polyarteritis nodosa of (Sinclair, Jr., and Nitsch), 898
elastic, lesions in, associated with hypertension, 310*
Arteries—Cont'd
intrapulmonary, and arterioles in coarctation of aorta associated with patent ductus arteriosus, pathology of (Edwards et al.), 205
peripheral, new treatment for relief of obliterative disease of, 924*
Arteriographic examination of lower extremity, some technical considerations in, 793*
Arterioles, cutaneous, in arm and leg in coarctation of aorta, changes in, 468*
pathology of intrapulmonary arteries and, in coarctation of aorta associated with patent ductus arteriosus (Edwards et al.), 205
Arteriosclerosis, canine, experimental, pathology of early lesions in, 462*
serum lipids in, 462*
cerebral, principal syndromes associated with, 471*
coronary, results of treatment of, with choline, 471*
significance of blood serum cholesterol instability in, 478*
does it develop by episodic stages? 469*
glomerular obsolescence in; identity and significance, 475*
observations on experimental production of, in guinea pig, 459*
of kidney, nature of hyaline material in, 470*
peripheral, use of radioactive sodium in diagnosis of peripheral circulation in, 469*
production of, in dogs by cholesterol and thiouracil feeding (Steiner et al.), 34
silica content of aortic wall in, 476*
Arteriovenous fistula of lung, 315*
pulmonary, hereditary hemorrhagic telangiectasis associated with, in two members of family, 799*
Arteritis, temporal, 143*
Artery, brachial, of normal subjects and patients with myasthenia gravis, effect of injection of acetylcholine into, 629*
conus: third coronary artery (Schlesinger et al.), 823
disease, coronary, 938 (B. Rev.)
Artery-aortic septal defect, pulmonary, pulmonary hemangioma with (Erf et al.), 766
Ashby marked red cell method and T 1824 hematocrit method in man, comparison of estimates of circulating red blood cell volume given by, 630*
Ataxia, Friedreich's myocarditis and (Hejtmancik et al.), 757
Atherohepatosis, experimental atheromatosis and, in ducks and geese: its reversibility and its clinical implications, 467*
Atheromatosis development in chicken, relationship of, to amount of cholesterol added to diet (Horlick and Katz), 336

Atheromatosis—Cont'd
experimental, and atherohepatosis in ducks and geese; its reversibility and its clinical implications, 467*
hamster as experimental animal for study of, 474*
rapid production of, in rabbits, 459*
Atherosclerosis, cholesterol, experimental, in alloxan diabetes in rabbit, studies on mechanism of inhibition of, 460*
of rabbits, mitotic activity in aortic lesions of, 635*
cholesterol-induced, in chick, development and metamorphosis of; effects of restricted dietary intake and of cessation of cholesterol feeding, 465*
of chicken, role of desiccated thyroid and potassium iodide in (Dauber et al.), 25
experimental, modification of, by means of intravenous detergents, 460*
fat absorption and; theory on development of atherosclerosis with ageing, 472*
in diabetes mellitus, study of, 475*
relationship of blood and liver cholesterol to, in different species, 463*
spontaneous and cholesterol-induced, and lipic metabolism in chick, studies on; effects of some lipotropic and hormonal factors, 466*
Atrial septal defect; study of intracardiac shunts, ventricular outputs, and pulmonary pressure gradient (Hickam), 801
septum, cause and effects of flow through defects of (Hull), 350
Auricular fibrillation, electric shock and, 636*
role of anemia in experimental production of heart block and, in dog (Horlick and Surtshin), 716
flutter during administration of cyclopropane and curare (Mahanna et al.), 301
tachycardia, paroxysmal, treatment of infant with, 444*
Auriculoventricular excitation, anomalous, electrocardiograms of unusual pattern in patient with (Roth and Doff), 614
Axis, electrical, mean, of heart, device for measuring (Topp and Rosenbaum), 130

B

Bacterial endocarditis, subacute, 935 (B. Rev.)
penicillin treatment of, 925*
report of case of reinfection, 927*
(*Streptococcus faecalis*), recovery from (Hein and Berg), 433
Beats, premature, occurring in angina pectoris induced by effort, probably grave significance of, 795*
Bernheim's syndrome, massive hypertrophy of heart with special reference to, 794*
Biomicroscopy of conjunctival vessels in hypertension (Lack et al.), 654
Blood and liver cholesterol, relationship of, to atherosclerosis in different species, 463*
cell, red, circulating, volume, comparison of estimates of, given by Ashby marked red cell method and T 1824 hematocrit method in man, 630*
observations on estimate of, in man given by T 1824 and hematocrit, with special reference to uncorrected dye loss from circulation, 631*
volume, comparison of results of measurements of, by direct and indirect techniques, 798*
coagulation, penicillin, streptomycin, Dicumarol, and; thromboplastic properties of penicillin antibiotics, 148*
flow, coronary, oxygen consumption, and efficiency of left ventricle in man, measurement of (Bing et al.), 1
hepatic, and splanchnic oxygen consumption in heart failure, estimation of, 306*
in extremities in cases of coarctation of aorta, studies on: determinations before and after excision of coarctate region, 634*
of, in extremities, effects of diathermy on, 153*
through chambers of heart in human beings, new method for studying: radiocardiography, 445*
human, effect of aminophyllin on coagulation of, 628*
infusion, plasma and, following myocardial infarction (Sampson and Singer), 54
observations concerning effects of, upon action of digitalis glycoside, 796*
of hypertensive patients, on occurrence of renin in (Mylon and Freedman), 509
plasma and serum in normal children, electrophoretic patterns in (V); immunologic and biochemical studies in infants and children with special reference to rheumatic fever, 931*
in rheumatic children, electrophoretic patterns of (VI); immunologic and biochemical studies in infants and children with special reference to rheumatic fever, 931*
pressure and heart disease, variation of, with age, and correlation of blood pressure with height and weight, 148*
and renal circulation of dogs with experimental neurogenic hypertension, effects of repeated oral doses of quinine and quinidine on, 449*
and tetraethylammonium chloride response, effect of sodium chloride depletion of, in hypertension, 928*
arterial effect of low sodium diet and rice diet on, 934*
maintenance in normal and toxemic pregnancy using tetraethylammonium chloride, evaluation of neurogenic and humoral factors in, 927*

Blood pressure—Cont'd
radial or brachial intra-arterial, alterations of, and of electrocardiogram induced by tilting, 144*
supply to lungs, experimental approach to problem of increasing, 446*
venous, rate of flow of, in legs measured with radioactive sodium 932*
viscosity, intravascular, digital, effect of anemia and polycythemia on, 155*
Bronchopulmonary disease, chronic, P wave in precordial leads in, 312*
Brucella melitensis endocarditis (Beebe and Meneely, Jr.), 788
Bundle branch block, pathogenesis of, 315*
right, incomplete, precordial electrocardiogram in (Barker and Valencia), 376

C

Calcification as diagnostic sign of syphilitic aortitis (Thorner et al.), 641
Capillary fragility and diabetic retinitis, 312*
pressure, pulmonary, in animals estimated by venous and arterial catheterization, 449*
strength tests in scurvy and their reactions to vitamin C and vitamin P therapy, 309*
Cardiac abnormalities, value of routine fluorograms as measure for detecting, 798*
dysfunction in hyperthyroidism (Griswold and Keating, Jr.), 813
lesions in thiamine deficiency, 639*
mechanism during anesthesia and operation in patients with congenital heart disease and cyanosis, 153*
"myxoma," mitral stenosis and insufficiency produced by (Weinstein and Arata), 781
output in man, Fick and dye injection methods of measuring, 314*
septa, closure of defects of, 624*
Cardiology, introduction to, 936 (B. Rev.)
Cardiomegaly, hyperplastic and hypertrophic, infantile, idiopathic (congenital cardiac hypertrophy) (Race and Black-Schaffer), 501
Cardiopatios congenitas de la infancia, 936 (B. Rev.)
Cardiovascular disease, relation of, to apoplexy (Hicks and Black), 528
dynamics effect on, in normotensive conditions: drastic food restriction, 140*
syphilis, penicillin therapy of (Flaum and Thomas), 361
Caronamide and penicillin: serum levels in human beings, following multiple doses of drugs, 926*
Carotid sinus reflex, hyperactive, subjective manifestations of, 452*
syndrome, unusual features in case of (de Vries and Halpern), 295
Case-taking, clinical. Guides for study of patients. History-taking and physical examination or semiology of disease in various systems, 940 (B. Ack'd)
Catheterization, cardiac, in congenital heart disease, 938 (B. Rev.)
venous and arterial, pulmonary capillary pressure in animals estimated by, 449*
Causalgia following gunshot injuries of nerves, 138*
III. General discussion, 638*
Cavities of right side of human heart, observations on potential variations of (Kert and Hoobler), 97
Cerebral arteriosclerosis, principal syndromes associated with, 471*
Chest and heart, 156 (B. Rev.)
Chicken, relationship of atheromatosis development in, to amount of cholesterol added to diet (Horlick and Katz), 336
role of desiccated thyroid and potassium iodide in cholesterol-induced atherosclerosis of (Dauber et al.), 25
Children, diffuse interstitial myocarditis in, 797*
Chloroform, ventricular irregularities induced by sympathoadrenal discharge and, 930*
Cholesterol, amount of, added to diet, relationship of atheromatosis development in chicken to (Horlick and Katz), 336
and thiouracil feeding, production of arteriosclerosis in dogs by (Steiner et al.), 34
atherosclerosis, experimental, in alloxan diabetes in rabbit, studies on mechanism of inhibition of, 460*
of rabbits, mitotic activity in aortic lesions of, 635*
blood and liver, relationship of, to atherosclerosis in different species, 463*
serum, instability in coronary arteriosclerosis, significance of, 478*
feeding, effects of restricted dietary intake and of cessation of; development and metamorphosis of cholesterol-induced atherosclerosis in chick, 465*
plasma and liver, effect of graded dosages of iodide on, of normal, cholesterol-fed, and thyroidectomized rabbits, 479*
tissue, distribution, thyroid activity and, 473*
Cholesterol-induced atherosclerosis of chicken, role of desiccated thyroid and potassium iodide in (Dauber et al.), 25
Choline, results of treatment of coronary arteriosclerosis with, 471*
Circulation, collateral, (anatomical aspects), 940 (B. Ack'd)
peripheral and epinephrine sensitization following sympathectomy, studies on (Deterling, Jr., and Essex), 248
use of radioactive sodium in diagnosis of, in peripheral arteriosclerosis, 469*
regional measurement of, by local clearance of radioactive sodium (Kety), 321

Circulation—Cont'd
renal, blood pressure and, of dogs with experimental neurogenic hypertension, effects of repeated oral doses of quinine and quinidine on, 449*
shock and allied forms of failure of, 939 (B. Rev.)
time, aminophyllin determination of, 443*
in man, use of acetylcholine in objective determination of, 796*
Circulatory arrest, acute, from ventricular fibrillation for twenty-seven minutes with complete recovery, 142*
failure, peripheral, acute, caused by acute venous thrombosis, 444*
stasis, control of, by electrical stimulation of large muscle groups, 448*
Claudication, intermittent, occurrence of paroxysmal hypertension in patients with (Malinow et al.), 702
Clotting time, relationship between heparin and, 625*
Coarctation, acquired, of aorta near diaphragm, 792*
of aorta, 316*
associated with patent ductus arteriosus, pathology of intrapulmonary arteries and arterioles in (Edwards et al.), 205
at unusual sites (Bahnson et al.), 905
congenital mitral stenosis and systemic right ventricle with associated pulmonary vascular changes frustrating surgical repair of patent ductus arteriosus and (Swan et al.), 914
pathologic considerations in, 633*
preoperative and postoperative studies of intraradial and intrafemoral pressures in patients with, 634*
sounds and murmurs in (Wells et al.), 69
studies on blood flow in extremities in cases of: determinations before and after excision of coarctate region, 634*
surgical treatment of, 634*
and physiopathology of, 623*
value of roentgen diagnosis in, 633*
Cold, ventricular fibrillation induced by (Hoff and Stansfield), 193
Collateral circulation (anatomical aspects), 940 (B. Ack'd)
Congestive heart failure, insensible loss of water in, 795*
renal and ciculatory factors in edema formation of, 928*
Conjunctival vessels biomicroscopy of, in hypertension (Lack et al.), 654
Contusion of heart, delayed death following (Kulka), 438
Conus artery: third coronary artery (Schlesinger et al.), 823
Coronary arteries, anomalies of, 632*
improved method for visualizing, at post mortem (Scott et al.), 881
of newborn infants, necrosis in (Gruenwald), 889
polyarteritis nodosa of (Sinclair, Jr., and Nitsch), 898
Coronary—Cont'd
arteriosclerosis, results of treatment of, with choline, 471*
significance of blood serum cholesterol instability in, 478*
artery disease, 938 (B. Rev.)
high precordial leads in normal subject and in patients with, 632*
third: conus artery (Schlesinger et al.), 823
blood flow, oxygen consumption, and efficiency of left ventricle in man, measurement of (Bing et al.), 1
dilator drugs, further studies on antifibrillatory action of, 627*
disease, heart muscle and electrocardiogram in I. Survey of standards and methods for obtaining anatomic data requisite for clinicopathologic correlation (Sheldon and Saÿen), 517
II. Difficulties of description and illustration of ventricular muscle lesions, with method for graphic representation in myocardial map (Saÿen and Sheldon), 688
flow, relationship between reduction in, and appearance of electrocardiographic changes (Wégria et al.), 90
heart disease, 935 (B. Rev.)
sclerosis in infancy, 448*
Curare, auricular flutter during administration of cyclopropane and (Mahanna et al.), 301
Cyclopropane and curare, auricular flutter during administration of (Mahanna et al.), 301
Cytochrome C: intravenous administration in man, 135*

D

Death, delayed, following contusion of heart (Kulka), 438
Deformations, mechanical, new method for electrical recording of, 933*
Depressor reflexes from heart, 447
Desoxycorticosterone acetate (DCA), potentiation of hypertensive effects of, by various sodium salts, 313*
Detergents, intravenous, modification of experimental atherosclerosis by means of, 460*
Dextrocardia, congenital, isolated, case of, without inversion of chambers and associated with left ventricular hypertrophy and anteroseptal myocardial infarction, 637*
Diabetes mellitus, study of atherosclerosis in, 475*
vascular problem in, 468*
Diabetic retinitis, capillary fragility and, 312*
Diaphragm, acquired coarctation of aorta near, 792*
Diathermy, effects of, on flow of blood in extremities, 153*
Dicumarol absorption, relationship of, to gastric free hydrochloric acid (LaTona and LeFevre), 743

Dicumarol—Cont'd
effect of heparin and, on sludge formation, 445*
on erythrocyte sedimentation rate in normal men, 933*
effects of, on electrocardiogram, 145*
in experimental myocardial infarction, 145*
penicillin, streptomycin, and blood coagulation; thromboplastic properties of penicillin antibiotics, 148*
Dicumarol-induced hypoprothrombinemia in rats, effect of vitamin K on, 930*
Dietary intake, restricted, effects of, and of cessation of cholesterol feeding; development and metamorphosis of cholesterol-induced atherosclerosis in chick, 465*
Digitalis glycoside, observations concerning effects of blood upon action of, 796*
Digitoxin: its evaluation for initial digitalization of patient with congestive heart failure, 626*
poisoning, 137*
therapy, abnormal rapid rhythms associated with, 799*
Diphtheria, electrocardiographic changes in, 137*
Dipole, artificial, electrical axis of standard and thoracic leads obtained by means of, 632*
Doublet theory and nature of extrinsic and intrinsic deflection, remarks on; clinical and experimental observations on precordial leads and on changing electrical field and spontaneous electrical axes, 636*
Drugs, dilator, coronary, further studies on antifibrillatory action of, 627*
Dye injection, Fick and, methods of measuring cardiac output in man, comparison of, 314*

E

Edema formation of congestive heart failure, renal and circulatory factors in, 928*
role of sodium in production of, 318*
Electric shock and auricular fibrillation, 636*
Electrical axis, mean, of heart, device for measuring (Topp and Rosenbaum), 130
of standard and thoracic leads obtained by means of artificial dipole, 632*
field, changing, and spontaneous electrical axes, clinical and experimental observations on precordial leads and on; remarks on doublet theory and nature of extrinsic and intrinsic deflection, 636*
recording of mechanical deformations, new method for, 933*
stimulation of large muscle groups, control of circulatory stasis by, 448*
Electrocardiogram, alterations of radial or brachial intra-arterial blood pressure and of, induced by tilting, 144*
Electrocardiogram—Cont'd
effect of Dicumarol on, 145*
heart muscle and, in coronary disease. I. Survey of standards and methods for obtaining anatomic data requisite for clinicopathologic correlation (Sheldon and Saÿen), 517
II. Difficulties of description and illustration of ventricular muscle lesions with method for graphic representation in myocardial map (Saÿen and Sheldon), 688
normal unipolar precordial and limb lead (Sokolow and Friedlander), 665
precordial, in incomplete right bundle branch block (Barker and Valencia), 376
nature of, 798*
variability of, in normal young men (Simonson et al.), 407
Electrocardiograms, abnormal, in absence of demonstrable heart disease, 149*
esophageal, evaluation of, in diagnosis of healed posterior myocardial infarction, 794*
of unusual pattern in patient with anomalous auriculoventricular excitation (Roth and Doff), 614
Electrocardiographic and pathologic findings in posterior infarction, correlation of (V) (Myers et al.), 547
posterolateral infarction, correlation of (VI) (Myers et al.), 837
changes in diphtheria, 137*
relationship between reduction in coronary flow and appearance of (Wégria et al.) 90
serial, in young adults with acute rheumatic fever, 152*
correlation: roentgen cardiac kymography, 311*
manifestations of potassium intoxication, 934*
Electrocardiography, atlas of, 937 (B. Rev.)
clinical, some supplementary leads in, 940 (B. Ack'd)
direct, of human heart and intrathoracic electrocardiography, 936 (B. Rev.)
primer of, 940 (B. Rev.)
Electrophoretic pattern of serum protein, simultaneous studies on serum lipids and, in man: (1) action of inositol and other substances, 467*
patterns in blood plasma and serum in normal children (V); immunologic and biochemical studies in infants and children with special reference to rheumatic fever, 931*
of blood plasma and serum in rheumatic children (VI); immunologic and biochemical studies in infants and children with special reference to rheumatic fever, 931*
Embolism, air, arterial (Durant et al.), 481
after penicillin-oil-beeswax, 143*
aortic, 925*
pulmonary, venous thrombosis and, 639*
without infarction, 450*

Embolus, pulmonary, treatment of, by stellate block, 151*
saddle, of aorta; report of successful embolectomy, 139*
Endocarditis, bacterial, subacute, 935 (B. Rev.)
due to *Hemophilus parainfluenzae*, 140*
penicillin treatment of, 925*
report of case of reinfection, 927*
(*Streptococcus fecalis*), recovery from (Hein and Berg), 433
Brucella melitensis (Beebe and Meneely, Jr.), 788
enterococcal, 147*
gonococcic, penicillin therapy of (Dorset et al.), 610
malignant, acute, from pneumococcus, 635*
Pseudomonas septicemia and, 137*
Enterococcal endocarditis, 147*
Epinephrine, intracardiac, effect of: heart in terminal state, 799*
sensitization, studies on peripheral circulation and, following sympathectomy (Deterling, Jr., and Essex), 248
shock, pheochromocytoma with symptoms of, 315*
Erythrocyte sedimentation rate in normal men, effect of Dicumarol on, 933*
Esophageal electrocardiograms, evaluation of, in diagnosis of healed posterior myocardial infarction, 794*
Estrogens, effect of, upon partition of serum lipids in female patients, 472*
Excitation, auriculoventricular, anomalous, electrocardiograms of unusual pattern in patient with (Roth and Doff), 614
Extremity, lower, some technical considerations in arteriographic examination of, 793*

F

Fat absorption and atherosclerosis; theory on development of atherosclerosis with ageing, 472*
deposition, further studies on action of antilipfanogen in preventing, 465*
tolerance curves in rat and rabbit using I^{131}, 479*
tests in coronary thrombosis, 477*
Fibrillation, auricular, electric shock and, 636*
role of anemia in experimental production of heart block and, in dog (Horlick and Surtshin), 716
ventricular, acute circulatory arrest from, for twenty-seven minutes with complete recovery, 142*
induced by cold (Hoff and Stansfield), 193
paroxysmal, with recovery, 308*
Fick and dye injection methods of measuring cardiac output in man, 314*
Finger capillaries in schizophrenia and manic-depressive psychoses, studies of, 145*
Fistula, arteriovenous, pulmonary, hereditary hemorrhagic telangiectasis associated with, in two members of family, 799*
Fluorocardiography, studies of: tracings of left ventricle in myocardial infarction, 308*
Fluorograms, routine, value of, as measure for detecting cardiac abnormalities, 798*
Flutter, auricular, during administration of cyclopropane and curare (Mahanna et al.), 301
Food restriction, drastic effect on cardiovascular dynamics in normotensive and hypertensive conditions, 140*
Friedreich's ataxia, myocarditis and (Hejtmancik et al.), 757

G

Glomerular obsolescence in arteriosclerosis; identity and significance, 475*
Glycosides, cardiac, effects of, upon dynamics of circulation in congestive heart failure, 155*
Gonococcic endocarditis, penicillin therapy of (Dorset et al.), 610
Gunshot injuries of nerves, causalgia following, 138*

H

Hamster as experimental animal for study of atheromatosis, 474*
Heart block and auricular fibrillation in dog, role of anemia in experimental production of (Horlick and Surtshin), 716
complete, congenital, complicating pregnancy, 146*
in osteitis deformans, 316*
influence of vagal activity on (Messer et al.), 732
ventricular complexes in, 317*
chest and, 156 (B. Rev.)
delayed death following contusion of (Kulka), 438
depressor reflexes from, 447*
device for measuring mean electrical axis of heart (Topp and Rosenbaum), 130
disease, congenital, cardiac catheterization in, 938 (B. Rev.)
coronary, 935 (B. Rev.)
demonstrable, abnormal electrocardiograms in absence of, 149*
hoarseness in, 137*
statistical studies of. I. Important factors in heart disease mortality trends, 445*
treatment of, 935 (B. Rev.)
variation of blood pressure and, with age, and correlation of blood pressure with height and weight, 148*
diseases, childhood mortality from rheumatic fever and, 307*
failure, congestive, effects of cardiac glycosides upon dynamics of circulation in, 155*
insensible loss of water in, 795*
its evaluation for initial digitalization of patient with: digitoxin, 626*

Heart failure—Cont'd
renal and circulatory factors in edema formation of, 928*
fetal, human, study of specialized heart tissue at various stages of development of, 148*
herniation of, 925*
human, direct electrocardiography of, and intrathoracic electrocardiography, 936 (B. Rev.)
observations on potential variations of cavities of right side of (Kert and Hoobler), 97
in terminal state: effect of intracardiac epinephrine, 799*
massive hypertrophy of, with special reference to Bernheim's syndrome, 794*
muscle and electrocardiogram in coronary disease. I. Survey of standards and methods for obtaining anatomic data requisite for clinicopathologic correlation (Sheldon and Saijen), 517
II. Difficulties of description and illustration of ventricular muscle lesions, with method for graphic representation in myocardial map (Saijen and Sheldon), 688
infarcted, histology of, 473*
mammalian, regenerative capacity of, 317*
primary amyloidosis of (Hulbert and Meyer), 604
revascularization of, 624*
sarcoidosis involving, in case of sudden death, 638*
spontaneous rupture of, due to myocardial infarction, 797*
tissue, specialized, study of, at various stages of development of human fetal heart, 148*
Hemangioma, pulmonary, with pulmonary artery-aortic septal defect (Erf et al.), 766
Hematocrit, observations on estimate of circulating red blood cell volume in man given by T 1824 and, with special reference to uncorrected dye loss from circulation, 631*
Hemophilus parainfluenzae, subacute bacterial endocarditis due to, 140*
Heparin and clotting time, relationship between, 625*
and Dicumarol, effect of, on sludge formation, 445*
Hepatic blood flow and splanchnic oxygen consumption in heart failure, estimation of, 306*
Herniation of heart, 925*
Herzens, Röntgendiagnostik des, und der grossen Gefasse, 937 (B. Rev.)
Hexosamine levels, plasma, in acute rheumatic fever (Rosenberg and Schloss), 872
Hoarseness in heart disease, 137*
Hormonal factors, some lipotropic and, effects of; studies on spontaneous and cholesterol-induced atherosclerosis and lipid metabolism in chick, 466*
Hyaline material in arteriosclerosis of kidney, nature of, 470*
Hydrochloric acid, gastric free, relationship of Dicumarol absorption to (LaTona and LeFevre), 743
Hyperplastic and hypertrophic cardiomegaly, infantile idiopathic, (congenital cardiac hypertrophy) (Race and Black-Schaffer), 501
Hypertension and unilateral renal disorder, nephrectomy in, 629*
arterial, effect of tetraethylammonium in, 934*
intramedullary section of vasomotor pathways as treatment of, 447*
biomicroscopy of conjunctival vessels in (Lack et al.), 654
caused by unilateral kidney disease, 138*
effect of sodium chloride depletion on blood pressure and tetraethylammonium chloride response in, 928*
essential, surgical treatment of. IV. Case selection and technique as influencing results, 638*
experimental, vascular lesions in, 464*
hazards of thiocyanate therapy in, 627*
human parabiotic pygopagus twins with hypertension: report of case with clinical, psychologic, and endocrinologic observations, 792*
lesions in elastic arteries associated with, 310*
neurogenic, experimental, effects of repeated oral doses of quinine and quinidine on blood pressure and renal circulation of dogs with, 449*
paroxysmal, associated with tabes dorsalis, 797*
occurrence of, in patients with intermittent claudication (Malinow et al.), 702
renal, malignant, experimental, effect of crude renal extracts and purified renin on vascular lesions in, 478*
origin of, 157 (B. Rev.)
Hypertensive effects of desoxycorticosterone acetate (DCA), potentiation of, by various sodium salts, 313*
patient, water tolerance of; its relation to operability (de Takats and Fowler), 234
patients, normal and, effects of adrenalin in, in relation to mechanism of sustained pressure elevations, 136*
on occurrence of renin in blood of (Mylon and Freedman), 509
Hyperthyroidism, cardiac dysfunction in (Griswold and Keating, Jr.), 813
Hypertrophic cardiomegaly, idopathic infantile hyperplastic and (congenital cardiac hypertrophy) (Race and Black-Schaffer), 501
Hypertrophy, cardiac, question of, in residents of high altitudes, 139*
massive, of heart with special reference to Bernheim's syndrome, 794*
ventricular, left, and anteroseptal myocardial infarction, case of isolated congenital dextrocardia without inversion of chambers and associated with, 637*
right, ventricular complex in, as obtained by unipolar precordial and limb leads (Sokolow and Lyon), 273

Hypnosis and venous pressure, 309*
Hypocalcemia and hypopotassemia, differentiation of changes in Q-T interval in (Ernstene and Proudfit), 260
Hypopotassemia, differentiation of changes in Q-T interval in hypocalcemia and (Ernestene and Proudfit), 260
Hypoprothrombinemia, Dicumarol-induced, in rats, effect of vitamin K on, 930*
Hypothermal injury, histologic sequences of degeneration and repair of rabbit aorta following, 464*

I

I^{131}, fat tolerance curves in rat and rabbit using, 479*
Infancia, cardiopatias congenitas de la, 936 (B. Rev.)
Infants, newborn and young, isolated myocarditis in (Lind and Hultquist), 123
necrosis in coronary arteries of (Gruenwald), 889
Infarction, hemorrhagic, of spinal cord and complete paraplegia, dissecting aneurysm of aorta with (Scott and Sancetta), 747
myocardial, acute, effect of anticoagulants on incidence of thromboembolic complications in, 636*
anteroseptal, case of isolated congenital dextrocardia without inversion of chambers and associated with left ventricular hypertrophy and, 637*
coronary occlusion and, found post mortem at Massachusetts General Hospital during twenty-year period from 1926 to 1945 inclusive, note on, 451*
experimental, Dicumarol in, 145*
immediate sequelae of; their relation to prognosis, 136*
plasma and blood infusion following (Sampson and Singer), 54
posterior, healed, evaluation of esophageal electrocardiograms in diagnosis of, 794*
prognosis in. I. Prognosis after acute stage, 635*
spontaneous rupture of heart due to, 797*
tracings of left ventricle in: studies of fluorocardiography, 308*
posterior, correlation of electrocardiographic and pathologic findings in (Myers et al.), 547
posterolateral, correlation of electrocardiographic and pathologic findings in (VI) (Myers et al.), 837
pulmonary embolism without, 450*
Inositol and other substances, action of (1): simultaneous studies on serum lipids and electrophoretic pattern of serum protein in man, 467*
Interatrial septal defect (Cosby and Griffith), 80
Internal diseases, thrombosis as complication of, 311*
medicine, fundamentals of, 939 (B. Rev.)
Intracardiac epinephrine, effect of: heart in terminal state, 799*
shunts, ventricular outputs, and pulmonary pressure gradient, study of; atrial septal defect (Hickam), 801
Intrapulmonary arteries and arterioles in coarctation of aorta associated with patent ductus arteriosus, pathology of (Edwards et al.), 205
Intrathoracic electrocardiography, direct electrocardiography of human heart and, 936 (B. Rev.)
operations, anoxia during, 628*
Intravenous detergents, modification of experimental atherosclerosis by means of, 460*
Iodide, effect of graded dosages of, on plasma and liver cholesterol of normal, cholesterol-fed, and thyroidectomized rabbits, 479*

K

7-Ketocholesterol in serum, method for estimation of, 474*
Kidney disease, unilateral, hypertension caused by, 138*
nature of hyaline material in arteriosclerosis of, 470*
Kymography, cardiac, roentgen: electrocardiographic correlation, 311*

L

Lead, limb, normal unipolar precordial and, electrocardiogram (Sokolow and Friedlander), 665
Leads, limb, unipolar precordial and, ventricular complex in right ventricular hypertrophy as obtained by (Sokolow and Lyon), 273
precordial, clinical and experimental observations on, and on changing electrical field and the spontaneous electrical axes; remarks on doublet theory and nature of extrinsic and intrinsic deflection, 636*
high, in normal subjects and in patients with coronary artery disease, 632*
P wave in, in chronic bronchopulmonary disease, 312*
position of (Rosenburg and Agress), 593
standard and thoracic, electrical axis of, obtained by means of artificial dipole, 632*
supplementary, some, in clinical electrocardiography, 940 (B. Ack'd)
Libman-Sacks syndrome, 309*
Limb lead, normal unipolar precordial and, electrocardiogram (Sokolow and Friedlander), 665
leads, unipolar precordial and, ventricular complex in right ventricular hypertrophy as obtained by (Sokolow and Lyon), 273
Lipid metabolism, studies on spontaneous and cholesterol-induced atherosclerosis and, in chick; effects of some lipotropic and hormonal factors, 466*

Lipotropic and hormonal factor, some effects of; studies on spontaneous and cholesterol-induced atherosclerosis and lipid metabolism in chick, 466*
Liver, blood and, cholesterol, relationship of, to atherosclerosis in different species, 463*
plasma and, cholesterol, effect of graded dosages of iodide on, of normal, cholesterol-fed, and thyroidectomized rabbits, 479*
Lung, arteriovenous aneurysm of, 446*
fistula of, 315*
Lungs, experimental approach to problem of increasing blood supply to, 446*

M

Manic-depressive psychoses, studies of finger capillaries in schizophrenia and, 145*
Meals, case of angina pectoris precipitated chiefly by tobacco smoking and (Ahn and Gühle), 775
Mediastinitis anterior chronica, 629*
Medionecrosis of aorta, 639*
Men, young, normal, variability of electrocardiogram in (Simonson et al.), 407
Metabolic studies in coronary thrombosis, 477*
Metabolism and excretion of salicylate, effect of para-aminobenzoic acid on, 929*
Methemoglobin-tagged cells, measurement of circulating red cell volume with, 314*
Mitotic activity in aortic lesions of experimental cholesterol atherosclerosis of rabbits, 635*
Mitral stenosis and insufficiency produced by cardiac "myxoma" (Weinstein and Arata), 781
congenital, and systemic right ventricle with associated pulmonary vascular changes frustrating sugical repair of patent ductus arteriosus and coarctation of aorta (Swan et al.), 914
experimental study of pulmonary-azygos venous anastomosis (Swan), 367
(Lutembacher's syndrome), familial interauricular septal defect with, 795*
surgical treatment of; valvuloplasty, 932*
Murmurs, sounds and, in coarctation of aorta (Wells et al.), 69
Muscle, heart, and electrocardiogram in coronary disease. I. Survey of standards and methods for obtaining anatomic data requisite for clinicopathologic correlation (Sheldon and Saijen), 517
II. Difficulties of description and illustration of ventricular muscle lesions, with method for graphic representation in myocardial map (Saijen and Sheldon), 688
infarcted, histology of, 473*
Myasthenia gravis, effect of injection of acetylcholine into brachial artery of normal subjects and patients with, 629*
Myocardial changes in poliomyelitis, 637*
infarction, acute, effect of anticoagulants on incidence of thromboembolic complications in, 636*
immediate sequelae of; their relationship to prognosis, 136*
plasma and blood infusion following (Sampson and Singer), 54
posterior, healed, evaluation of esophageal electrocardiograms in diagnosis of, 794*
prognosis in. I. Prognosis after acute stage, 635*
spontaneous rupture of heart due to, 797*
map, difficulties of description and illustration of ventricular muscle lesions, with method for graphic representation in (II); heart muscle and electrocardiogram in coronary disease (Saijen and Sheldon), 688
Myocarditis and Friedreich's ataxia (Hejtmancik et al.), 757
interstitial, diffuse, in children, 797*
isolated (Fieldlers), 153*
in newborn and young infants (Lind and Hultquist), 123
Myoglobin and its occurrence in man, on, 940 (B. Rev.)
"Myxoma," cardiac, mitral stenosis and insufficiency produced by (Weinstein and Arata), 781

N

Nail changes in functional and organic arterial disease, 443*
Necrosis in coronary arteries of newborn infants (Gruenwald), 889
Nephrectomy in hypertension and unilateral renal disorder, 629*

O

Obliterative disease of peripheral arteries, new treatment for relief of, 924*
Occlusion, arterial, acute, arterectomy in treatment of intractable pain following recovery from (Freeman et al.), 329
coronary, and myocardial infarction found post mortem at Massachusetts General Hospital during twenty-year period from 1926 to 1945 inclusive, note on, 451*
Oligemic shock, on certain aspects of nature and treatment of (Page), 161
Operability, its relation to; water tolerance of hypertensive patient (de Takats and Fowler), 234
Operation, cardiac mechanism during anesthesia and, in patients with congenital heart disease and cyanosis, 153*
Osteitis deformans, heart block in, 316*
Ouabain, comparison of, with strophanthidin-3-acetate by intravenous injection in man, 307*
Oxygen consumption, coronary blood flow, and efficiency of left ventricle in man, measurement of (Bing et al.), 1

Oxygen consumption—Cont'd
splanchnic, estimation of hepatic blood flow and, in heart failure, 306*
therapy, effect of, on electrical sequence of events in cardiac cycle in children with acute rheumatic carditis, 150*
in acute rheumatic carditis in children, 150*
Oxyhemograph, control of anoxemia during surgical anesthesia with aid of, 623*

P

P wave in precordial leads in chronic bronchopulmonary disease, 312*
Pain, intractable, following recovery from acute arterial occlusion, arterectomy in treatment of (Freeman et al.), 329
Palmar arch, occupational aneurysm of, 147*
Paraplegia, complete, dissecting aneurysm of aorta with hemorrhagic infarction of spinal cord and (Scott and Sancetta), 747
Para-aminobenzoic acid, effect of, on metabolism and excretion of salicylate, 929*
Paroxysmal hypertension, occurrence of, in patients with intermittent claudication (Malinow et al.), 702
Patent ductus arteriosus and coarctation of aorta, congenital mitral stenosis and systemic right ventricle with associated pulmonary vascular changes frustrating surgical repair of (Swan et al.), 914
pathology of intrapulmonary arteries and arterioles in coarctation of aorta associated with (Edwards et al.), 205
prognosis of, in fifty-four nonoperated cases, 636*
Penicillin, Caronamide and: serum levels in human beings, following multiple doses of drugs, 926*
effect of tonsillectomy and administration of, on rheumatic and nonrheumatic fever patients, studies on rheumatic fever; observations on tonsillar carriers of hemolytic streptococci, 306*
streptomycin, Dicumarol, and blood coagulation; thromboplastic properties of penicillin antibiotics, 148*
therapy of cardiovascular syphilis (Flaum and Thomas), 361
of gonococcic endocarditis (Dorset et al.), 610
treatment of subacute bacterial endocarditis, 925*
Penicillin-oil-beeswax, embolism after, 143*
Periarteritis nodosa, 631*
Pericarditis, constrictive, chronic, 630*
tuberculous, 317*
Peripheral arteries, new treatment for relief of obliterative disease of, 924*
arteriosclerosis, use of radioactive sodium in diagnosis of peripheral circulation in, 469*
Peripheral—Cont'd
circulation and epinephrine sensitization following sympathectomy, studies on (Deterling, Jr., and Essex), 248
circulatory failure, acute, caused by acute venous thrombosis, 444*
resistance, local, asystolic arterial pressure gradient as measure of, 449*
Pheochromocytoma, 154*
use of tetraethylammonium bromide as diagnostic test for, 924*
with symptoms of epinephrine shock, 315*
Phonocardiography, modern, 307*
Pituitary insufficiency, anterior, (panhypopituitarism—Simmonds' disease), pituitary myxedema and congestive heart failure (myxedema heart); report of case and findings at necropsy, 452*
Plasma and blood infusion following myocardial infarction (Sampson and Singer), 54
and liver cholesterol, effect of graded dosages of iodide on, of normal, cholesterol-fed, and thyroidectomized rabbits, 479*
and serum, blood, in normal children, electrophorectic patterns in (V); immunologic and biochemical studies in infants and children with special reference to rheumatic fever, 931*
in rheumatic children, electrophoretic patterns of (VI); immunologic and biochemical studies in infants and children with special reference to rheumatic fever, 931*
hexosamine levels in acute rheumatic fever (Rosenberg and Schloss), 872
Platelet clumping, increased, in thromboembolic disease, 794*
Pneumococcus, acute malignant endocarditis from, 635*
Poliomyelitis, myocardial changes in, 637*
Polyarteritis nodosa of coronary arteries (Sinclair, Jr., and Nitsch), 898
Polycythemia, effect of anemia and, of digital intravascular blood viscosity, 155*
Post-tachycardia syndrome, clinical and anatomical study of, 313*
Potassium and sodium, distribution of, between serum and certain extracellular fluids in man, 315*
intoxication, electrocardiographic manifestations of, 934*
iodide, role of desiccated thyroid and, in cholesterol-induced atherosclerosis of chicken (Dauber et al.), 25
Precordial electrocardiogram in incomplete right bundle branch block (Barker and Valencia), 376
nature of, 798*
leads, high, in normal subjects and in patients with coronary artery disease, 632*
position of (Rosenburg and Agress), 593
unipolar, and limb leads, ventricular complex in right ventricular hypertrophy as obtained by (Sokolow and Lyon), 273

Precordial unipolar—Cont'd
normal, and limb lead electrocardiogram (Sokolow and Friedlander), 665
Pregnancy, congenital complete heart block complicating, 146*
toxemic, normal and, evaluation of neurogenic and humoral factors in blood pressure maintenance in, using tetraethylammonium chloride, 927*
Pregnant women, normal, duration of Q-T interval in (Benjamin), 119
Pressure, arterial, pulmonary (Rodbard et al.), 863
gradient, pulmonary, study of intracardiac shunts, ventricular outputs, and; atrial septal defect (Hickam), 801
Pressures, intraradial and intrafemoral, preoperative and postoperative studies of, in patients with coarctation of aorta, 634*
venous, in children in health and disease, 931*
Pseudomonas septicemia and endocarditis, 137*
Pulmonary arterial pressure (Rodbard et al.), 863
capillary pressure in animals estimated by venous and arterial catheterization, 449*
embolism, venous thrombosis and, 639*
pressure gradient, study of intracardiac shunts, ventricular outputs, and; atrial septal defect (Hickam), 801
stenosis, diagnosis of, by angiocardiography, 930*
vascular changes, associated, frustrating surgical repair of patent ductus arteriosus and coarctation of aorta, congenital mitral stenosis and systemic right ventricle with (Swan et al.), 914
vessels, anomalous, 628*
Pulmonary-azygos venous anastomosis, experimental study of: mitral stenosis (Swan), 367
Purpuric conditions, inconstancy and variability of vascular fragility test even in, 624*
Pygopagus, human parabiotic, twins with hypertension: report of case with clinical, psychologic, and endocrinologic observations, 792*
Pyrogen test, standardized, ageing as factor in renal hemodynamic response to, 476*

Q

Q-T interval, duration of, in normal pregnant women (Benjamin), 119
in hypocalcemia and hypopotassemia, differentiation of changes in (Ernstene and Proudfit), 260
in rheumatic fever, study of (Pokress and Goldberger), 423
Quinidine, effects of repeated oral doses of quinine and, on blood pressure and renal circulation of dogs with experimental neurogenic hypertension, 449*
Quinine and quinidine, effects of repeated oral doses of, on blood pressure and renal circulation of dogs with experimental neurogenic hypertension, 449*

R

Radioactive sodium, measurement of regional circulation by local clearance of (Kety), 321
rate of flow of venous blood in legs measured with, 932*
Radiocardiography: new method for studying blood flow through chambers of heart in human beings, 445*
Red blood cell volume, comparison of results of measurements of, by direct and indirect technique, 798*
cell volume, circulating, effect of administration of adrenaline on, 798*
measurement of with methemoglobin-tagged cells, 314*
Renal disorder, unilateral, nephrectomy in hypertension and, 629*
extracts, crude, and purified renin, effect of, on vascular lesions in experimental malignant renal hypertension, 478*
hemodynamic response to standardized pyrogen test, ageing as factor in, 476*
Renin, on occurrence of, in blood of hypertensive patients (Mylon and Freedman), 509
purified, effect of crude renal extracts and, on vascular lesions in experimental malignant renal hypertension, 478*
Revascularization of heart, 624*
Rheumatic carditis, acute, effect of oxygen therapy on electrical sequence of events in cardiac cycle in children with, 150*
in children, oxygen therapy in, 150*
fever, acute, plasma hexosamine levels in (Rosenberg and Schloss) 872
serial electrocardiographic changes in young adults with, 152*
and heart diseases, childhood mortality from, 307*
immunologic and biochemical studies in infants and children with special reference to. I. Role of genetic susceptibility, 444*
V. Electrophoretic patterns in blood plasma and serum in normal children, 931*
VI. Electrophoretic patterns of blood plasma and serum in rheumatic children, 931*
longevity in: based on experience of 1,042 children observed over period of thirty years, 926*
pathogenesis of, 450*
studies on; observations on tonsillar carriers of hemolytic streptococci; effect of tonsillectomy and administration of penicillin on rheumatic and nonrheumatic fever patients, 306*

Rheumatic fever—Cont'd
study of Q-T interval in (Pokress and Goldberger), 423
patients who served in Armed Forces, 1942-46, experience of, 135*
Rhythm, alternating nodal and sinus, in case of situs viscerum inversus, 631*
Rhythms, rapid, abnormal, associated with digitoxin therapy, 799*
Rice diet, effect of low sodium diet and, on arterial blood pressure, 934*
Roentgen diagnosis in coarctation of aorta, value of, 633*
Röntgendiagnostik des Herzens und der grossen Gefasse, 937 (B. Rev.)

S

Salicylate, effect of sodium bicarbonate on renal excretion of, 146*
excretion of, effect of para-aminobenzoic acid on metabolism and, 929*
Sarcoidosis involving heart in case of sudden death, 638*
Scalenus anticus syndrome treated by surgery and skeletal traction, 150*
Schizophrenia and manic-depressive psychoses, studies of finger capillaries in, 145*
Sclerosis, coronary, in chickens, etiology of, 466*
in infancy, 448*
Scurvy, capillary strength tests in, and their reactions to vitamin C and vitamin P therapy, 309*
Semiology, history-taking and physical examination or, of diseases in various systems. Clinical case-taking. Guides for study of patients, 940 (B. Ack'd)
Septal defect, artery-aortic, pulmonary, pulmonary hemangioma with (Erf et al.), 766
atrial; study of intracardiac shunts, ventricular outputs, and pulmonary pressure gradient (Hickam), 801
interauricular, familial, with mitral stenosis (Lutembacher's syndrome), 7 5*
interatrial, defect (Cosby and Griffith), 80
Septicemia, Pseudomonas, and endocarditis, 137*
Septum, atrial, cause and effects of flow through defects of (Hull), 350
Serotonin, crystalline, 445*
Serum, blood plasma and, in normal children, electrophoretic patterns in (V); immunologic and biochemical studies in infants and children with special reference to rheumatic fever, 931*
in rheumatic children, electrophoretic patterns of (VI); immunologic and biochemical studies in infants and children with special reference to rheumatic fever, 931*
disease in rabbits, effect of sodium salicylate upon, 143*
levels in human beings, following multiple doses of drugs: Caronamide and penicillin, 926*
Serum—Cont'd
lipids and electrophoretic pattern of serum protein in man, simultaneous studies on: (1) action of inositol and other substances, 467*
effect of estrogens upon partition of, in female patients, 472*
in experimental canine arteriosclerosis, 462*
method for estimation of 7-ketocholesterol in, 474*
Shock and allied forms of failure of circulation, 939 (B. Rev.)
oligemic, on certain aspects of nature and treatment of (Page), 161
Shunts, intracardiac, ventricular outputs, and pulmonary pressure gradient, study of; atrial septal defect (Hickam), 801
Silica content of aortic wall in arteriosclerosis, 476*
Sinus, carotid, syndrome, unusual features in case of (de Vries and Halpern), 295
Situs viscerum inversus, alternating nodal and sinus rhythm in case of, 631*
Smoking, tobacco, and meals, case of angina pectoris precipitated chiefly by (Ahn and Göhle), 775
Sodium bicarbonate, effect of, on renal excretion of salicylate, 146*
chloride depletion, effect of, on blood pressure and tetraethylamonium chloride response in hypertension, 928*
distribution of potassium and, between serum and certain extracellular fluids in man, 315*
low, diet and rice diet, effect of, on arterial blood pressure, 934*
radioactive, measurement of regional circulation by local clearance of (Kety), 321
rate of flow of venous blood in legs measured with, 932*
use of, in diagnosis of peripheral circulation in peripheral arteriosclerosis, 469*
role of, in production of edema, 318*
salicylate, effect of, upon serum disease in rabbits, 143*
Sounds and murmurs in coarctation of aorta (Wells et al.), 69
Spatial vectorcardiogram in man, observations on (Conway et al.), 537
Spinal cord, hemorrhagic infarction of, and complete paraplegia, dissecting aneurysm of aorta with (Scott and Sancetta), 747
Stellate block, treatment of pulmonary embolus by, 151*
Stenosis, mitral, and insufficiency produced by cardiac "myxoma" (Weinstein and Arata), 781
congenital, and systemic right ventricle with associated pulmonary vascular changes frustrating surgical repair of patent ductus arteriosus and coarctation of aorta (Swan et al.), 91

Stenosis, mitral—Cont'd
experimental study of pulmonary-azygos venous anastomosis (Swan), 367
(Lutembacher's syndrome), familial interauricular septal defect with, 795*
surgical treatment of; valvuloplasty, 932*
pulmonic, congenital, surgical procedures employed and anatomical variations encountered in treatment of, 793*
Streptomycin, penicillin, Dicumarol, and blood coagulation; thromboplastic properties of penicillin antibiotics, 148*
Stroke volume, some factors in regulation of, 313*
Strophanthidin-3-acetate, comparison of ouabain with, by intravenous injection in man, 307*
Surgical procedures employed and anatomical variations encountered in treatment of congenital pulmonic stenosis, 793*
Susceptibility, genic, role of (I); immunologic and biochemical studies in infants and children with special reference to rheumatic fever, 444*
"Sustained pressor principle," observations on, in different animal species, 314*
Sympathectomy, results of, and prognosis; thromboangiitis obliterans, 932*
studies on peripheral circulation and epinephrine sensitization following (Deterling, Jr., and Essex), 248
Sympathoadrenal discharge and chloroform, ventricular irregularities induced by, 930*
Syphilis, cardiovascular, penicillin therapy of (Flaum and Thomas), 361
Syphilitic aortitis, calcification as diagnostic sign of (Thorner et al.), 641

T

T 1824 and hematocrit, observations on estimate of circulating red blood cell volume in man given by, with special reference to uncorrected dye loss from circulation, 631*
hematocrit method, comparison of estimates of circulating red blood cell volume given by Ashby marked red cell method and, in man, 630*
Tabes dorsalis, paroxysmal hypertension associated with, 797*
Tachycardia, auricular, paroxysmal, treatment of infant with, 444*
Telangiectasis, hemorrhagic, hereditary, associated with pulmonary arteriovenous fistula in two members of family, 799*
Temperatures, body, varying, thermal gradients during, 925*
Tetraethylammonium bromide, use of, as diagnostic test for pheochromocytoma, 924*
chloride, evaluation of neurogenic and humoral factors in blood pressure maintenance in normal and toxemic pregnancy using, 927*
Tetraethylammonium chloride—Cont'd
response in hypertension, effect of sodium chloride depletion on blood pressure and, 928*
effect of, in arterial hypertension, 934*
Thermal gradients during varying body temperatures, 925*
Thiamin deficiency, cardiac lesions in, 639*
Thiocyanate therapy in hypertension, hazards of, 627*
Thiouracil feeding, production of arteriosclerosis in dogs by cholesterol and (Steiner et al.), 34
Thromboangiitis obliterans; results of sympathectomy and prognosis, 932*
Thromboembolic complications in acute myocardial infarction, effect of anticoagulants on incidence of, 636*
disease, increased platelet clumping in, 794*
Thrombosis as complication of internal diseases, 311*
coronary, fat tolerance tests in, 477*
metabolic studies in, 477*
venous, 638*
acute, acute peripheral circulatory failure caused by, 444*
and pulmonary embolism, 639*
Thyroid activity and tissue cholesterol distribution, 473*
desiccated, and potassium iodide, role of, in cholesterol-induced atherosclerosis of chicken (Dauber et al.), 25
Thyroidectomized rabbits, normal, cholesterol-fed, and, effect of graded dosages of iodide on plasma and liver cholesterol of, 479*
Thyroidectomy and viosterol feeding, vascular lesions in dog following, 463*
Tilting, alterations of radial or brachial intra-arterial blood pressure and of electrocardiogram induced by, 144*
Tissue, arterial, biology of, 461*
cholesterol distribution, thyroid activity and, 473*
Tobacco smoking and meals, case of angina pectoris precipitated chiefly by (Ahn and Göhle), 775
Tonsillectomy and administration of penicillin, effect of, on rheumatic and nonrheumatic fever patients, studies on rheumatic fever: observations on tonsillar carriers of hemolytic streptococci, 306*
Tuberculous pericarditis, 317*

U

Unipolar precordial and limb leads, ventricular complex in right ventricular hypertrophy as obtained by (Sokolow Lyon), 273
normal, and limb lead electrocardiogram (Sokolow and Friedlander), 665

V

Vagal activity, influence of, on heart block (Messer et al.), 732
Valvuloplasty; surgical treatment of mitral stenosis, 932*

Vascular changes, pulmonary, associated, frustrating surgical repair of patent ductus arteriosus and coarctation of aorta, congenital mitral stenosis and systemic right ventricle with (Swan et al.), 914
fragility test, inconstancy and variability of, even in purpuric conditions, 624*
lesions in dog following thyroidectomy and viosterol feeding, 463*
in experimental hypertension, 464*
problem in diabetes mellitus, 468*
Vectorcardiogram, spatial, in man, observations on (Conway et al.), 537
Venous anastomosis, pulmonary-azygos, experimental study of: mitral stenosis (Swan), 367
blood, rate of flow of, in legs measured with radioactive sodium, 932*
pressure, hypnosis and, 309*
pressures in children in health and disease, 931*
thrombosis, 638*
acute, acute peripheral circulatory failure caused by, 444*
Ventricle, left, efficiency of, measurement of coronary blood flow, oxygen consumption, and, in man (Bing et al.), 1
right, systemic, congenital mitral stenosis and, with associated pulmonary vascular changes frustrating surgical repair of patent ductus arteriosus and coarctation of aorta (Swan et al.), 914
Ventricular complex in right ventricular hypertrophy as obtained by unipolar precordial and limb leads (Sokolow and Lyon), 273
complexes in heart block, 317*
fibrillation induced by cold (Hoff and Stansfield), 193
paroxysmal, with recovery, 308*
irregularities induced by sympathoadrenal discharge and chloroform, 930*
muscle lesions, difficulties of description and illustration of, with method for graphic representation in myocardial map (II); heart muscle and electrocardiogram in coronary disease (Saijen and Sheldon), 688
outputs, intracardiac shunts, and pulmonary pressure gradient, study of; atrial septal defect (Hickam), 801
Viosterol feeding, vascular lesions in dog following thyroidectomy and, 463*
Vitamin K, effect of, on Dicumarol-induced hypoprothrombinemia in rats, 930*

W

Water, insensible loss of, in congestive heart failure, 795*
tolerance of hypertensive patient; its relation to operability (de Takats and Fowler), 234

MEDICAL LIBRARY

INDEX NUMBER

JAN 20 1950

VOL. 38 DECEMBER, 1949 No. 6

AMERICAN HEART JOURNAL

For the Study of the

CIRCULATION

THOMAS M. McMILLAN : : Editor-in-Chief

Associate Editors

WALLACE M. YATER
SAMUEL BELLET
MORRIS W. STROUD, III

EDITORIAL BOARD

EDGAR V. ALLEN
ALFRED BLALOCK
CLARENCE E. DE LA CHAPELLE
HARRY GOLDBLATT
TINSLEY R. HARRISON
T. DUCKETT JONES
LOUIS N. KATZ
CHARLES E. KOSSMANN
EUGENE M. LANDIS
JOHN K. LEWIS
H. M. MARVIN
JONATHAN C. MEAKINS
ROY W. SCOTT
ISAAC STARR
HELEN B. TAUSSIG
PAUL D. WHITE
FRANK N. WILSON
CHARLES C. WOLFERTH
IRVING S. WRIGHT

Published Monthly Under the Editorial Direction of The American Heart Association

Published and Copyrighted 1949 by The C. V. Mosby Company, St. Louis, U. S. A.

Contents on Inside Cover

American Heart Journal

CONTENTS FOR DECEMBER, 1949

Original Communications

Atrial Septal Defect. A Study of Intracardiac Shunts, Ventricular Outputs, and Pulmonary Pressure Gradient. John B. Hickam, M.D., Durham, N. C. 801

Cardiac Dysfunction in Hyperthyroidism. Dwight Griswold, M.D., and John H. Keating, Jr., M.D., New York, N. Y. 813

The Conus Artery: A Third Coronary Artery. Monroe J. Schlesinger, M.D., Paul M. Zoll, M.D., and Stanford Wessler, M.D., Boston, Mass. 823

VI. Correlation of Electrocardiographic and Pathologic Findings in Posterolateral Infarction. Gordon B. Myers, M.D., Howard A. Klein, M.D., and Tomiharu Hiratzka, M.D., Detroit, Mich. 837

The Pulmonary Arterial Pressure. S. Rodbard, Ph.D., F. Brown, M.D., and L. N. Katz, M.D., Chicago, Ill. 863

Plasma Hexosamine Levels in Acute Rheumatic Fever. Conrad Rosenberg, M.D., and Benjamin Schloss, Ph.D., New York, N. Y. 872

An Improved Method for Visualizing the Coronary Arteries at Post Mortem. R. W. Scott, M.D., A. F. Young, M.D., H. A. Zimmerman, M.D., and Ileen Kroh, B.S., Cleveland, Ohio 881

Necrosis in the Coronary Arteries of Newborn Infants. Peter Gruenwald, M.D., Brooklyn, N. Y. 889

Clinical Reports

Polyarteritis Nodosa of the Coronary Arteries. William Sinclair, Jr., M.D., Cleveland, Ohio, and Emilia Nitsch, M.D., Lakewood, Ohio 898

Coarctation of the Aorta at Unusual Sites. Henry T. Bahnson, M.D., Robert N. Cooley, M.D., and Robert D. Sloan, M.D., Baltimore, Md. 905

Congenital Mitral Stenosis and Systemic Right Ventricle With Associated Pulmonary Vascular Changes Frustrating Surgical Repair of Patent Ductus Arteriosus and Coarctation of the Aorta. Henry Swan, M.D., J. M. Trapnell, M.D., and John Denst, M.D., Denver, Colo. 914

Abstracts and Reviews

Selected Abstracts 924

Book Reviews 935

American Heart Association, Inc.

American Heart Association, Inc. 941

Index

Index 943

Vol. 38, No. 6, December, 1949, American Heart Journal is published monthly, except semi-monthly in April, by The C. V. Mosby Company, 3207 Washington Avenue, St. Louis 3, Missouri, entered as second class matter January 23, 1917 at the Post Office at St. Louis, Missouri, under the Act of March 3, 1879. Additional entry authorized at Jefferson City, Missouri. Subscription Price: United States, its Possessions, Pan-American Countries, $12.00; In Canada and other Foreign countries, $13.00. Printed in the U. S. A.